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ABSTRACT

A survey is presented of recently published periodical literature in the field of vaccine-preventable diseases. Information is provided on writings about: (1) measles; (2) rubella; (3) influenza; (4) diphtheria-pertussis-tetanus; and (5) other vaccine-preventable diseases. For each disease general information is covered, as well as clinical and laboratory information, epidemiology, and prevention and control. A selected bibliography accompanies each section. Abstracts are included of the most significant articles. Abstracts are also provided of writings on vaccines, antiviral agents, and toxoids, as well as general articles on immunization and health care delivery. (JD)

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SURVEY OF RECENT RESEARCH

NUMBER THREE

U.S. Department of Health and Human Services / Public Health Service / Centers for Disease Control

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IMMUNIZATION

Survey of Recent Research

NUMBER THREE

Issued December 1984

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Center for Prevention Services
Division of Immunization
Atlanta, Georgia 30333

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INTRODUCTION

Immunization: Survey of Recent Research presents a survey of recently published periodical literature in the field of vaccine-preventable diseases. Abstracts of the most significant articles are included as well as selected bibliographies of various topics in this field. Inclusion of an article in this publication does not imply endorsement by the United States Public Health Service of the article or of commercial drugs, products, or other therapeutic modalities mentioned.

In compiling these abstracts and bibliographies, use is made of the National Library of Medicine's interactive retrieval service, MEDLARS II. Under this system, some 2,600 foreign and domestic biomedical periodicals are searched for material dealing with or related to immunization and vaccine-preventable diseases. A description of the search parameters is included on the next page.

For each citation generated by the search, a decision is made to abstract, place in the bibliography, or omit. Initial selection of articles to abstract, and review of the final manuscript is done by the Surveillance, Investigations, and Research Branch, Division of Immunization. Technical Information Services, Center for Prevention Services, writes original abstracts where required, compiles and edits the manuscript, and oversees publication and distribution.

Abbreviations of periodical titles are those used by MEDLARS II, and listed in the National Library of Medicine's *List of Journals Indexed in Index Medicus*. The journals in which articles originally appeared should be checked for reprint addresses.

This publication is the third in a series, the first issue of which appeared in April 1983. Citations of nearly all of the periodical literature on the subjects of immunization and vaccine-preventable diseases published in 1983 have been reviewed for this issue.

Questions or comments concerning this publication are welcomed and should be directed to:

Technical Information Services
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Search Parameters

Searches of the National Library of Medicine's databanks are restricted to those articles dealing with human subjects and having one of the following terms as a major or minor descriptor:

amantadine
antiviral agents
bacterial vaccines
BCG vaccine
brucella vaccine
bulbar poliomyelitis
chickenpox
cholera vaccine
diphtheria
diphtheria toxoid
encephalitis, post-vaccinal
fungal vaccines
herpes zoster
herpes zoster, ocular
immunization
immunization, passive
immunization schedule
immunization, secondary
influenza
influenza vaccine
measles
measles vaccine
mumps
mumps vaccine
pertussis vaccine
plague vaccine
poliomyelitis
poliovirus vaccine
poliovirus vaccine, oral
rabies vaccine
ribavirin
rickettsial vaccines
rubella
rubella vaccine
smallpox
smallpox vaccine
staphylococcal toxoid
staphylococcal vaccines
subacute sclerosing panencephalitis
tetanus
tetanus toxoid
toxoids
typhoid-paratyphoid vaccines
vaccines
vaccines, attentuated
vaccinia
vaccination
viral vaccines
whooping cough

MEASLES

General

Measles: Summary of Worldwide Impact

F. Assaad. Rev Infect Dis 1983 May-Jun;5(3):452-9.

Author's abstract: Nearly every measles infection results in well-recognized clinical disease. In nonimmunized populations almost every child will get measles early in life. The universality of the disease in nonimmunized communities, particularly those in the developing world, has led to a more or less passive acceptance of measles as an unavoidable risk of early life. The clinical spectrum of measles ranges from a mild, self-limiting illness to a fatal disease. Conditions encountered mainly in the developing world, e.g., unfavorable nutrition, high risk of concurrent infection, and inadequate case management—particularly at home—favor the development of complications and adverse outcome. Conversely, good clinical management of an otherwise healthy child, a situation seen mostly in the developed world, greatly influences the course of the disease. Hence many in the medical profession believe that measles is a mild disease except among populations living under particularly unfavorable conditions. Measles vaccine is effective in preventing disease in the individual and in controlling it in the community if it is given at the critical age when maternal antibodies wane and the risk of natural infection increases sharply and if a high immunization rate is maintained in the target population. The experience with immunization, particularly in sub-saharan Africa, is rewarding: mothers who had previously accepted measles as an unavoidable risk clamor for immunization of their children once its effectiveness has been demonstrated. No reason exists for measles to claim its present toll of morbidity and mortality. With extension of the Expanded Program on Immunization of the World Health Organization, the impact of measles should progressively decline.

Congenital Measles—1982

B. Muhlbauer, L.M. Berns and A. Singer. Isr J Med Sci 1983 Nov;19(11):987-8.

Authors' abstract: Measles acquired in utero has a broad spectrum of illness, ranging from mild to rapidly fatal disease. We encountered two cases of perinatal measles during the 1982 epidemic. In both cases the mother became febrile 4 to 5 days before admission, and a typical morbilliform rash appeared a few hours prior to delivery. Physical examination of both infants was within normal limits. They were each treated with human serum globulin (0.25 ml/kg body weight). In one of them, a maculopapular rash appeared on the neck after 5 days, which rapidly spread to all the body. No catarrhal or constitutional signs were noted. Hyperbilirubinemia occurred in both infants, requiring an exchange transfusion in one. Both were discharged in excellent condition. Viral cultures were negative in both infants, while serological studies revealed hemagglutination inhibition antibodies in rising titers.

Measles: The Epidemiology and Control of an Outbreak

K.M. Poi. J Am Coll Health 1983 Feb;31(4):158-61.

Author's abstract: The implementation of rubeola immunization programs has resulted in a greater than 90% decrease in the number of measles' cases reported yearly. However, a shift in the susceptible age group has occurred. Recent outbreaks have been reported in adolescent and college populations. Concurrent and retrospective analysis of experiences in one such outbreak demonstrate the epidemiology of measles in young adults and the success of an aggressive control program. At the time of the outbreak, approximately 40,000 students were enrolled at the University of Wisconsin/Madison. Using several criteria, up to 3,500 students were estimated to be

susceptible to the disease. A total of 19 cases were identified. Interviews established a specific source of exposure for 13 of the 19. In an eight-day period, over 3,000 individuals were immunized, limiting the outbreak to four generations. The experience of others has suggested a high incidence of adverse reactions to rubeola vaccine. This was not the experience in this program.

Clinical and Laboratory

Severe Measles: Some Unanswered Questions

D. Morley. Rev Infect Dis 1983 May-Jun;5(3):460-2.

Author's abstract: The severity of measles is greatest in the developing countries, where a high proportion of children have nutritional deficiencies. Nutritional deficiencies may play a part in the complications that result from measles infection. Nutritional deficiencies may also be the reason for the young age at which infection is found in children in developing countries; the child with severe measles and an immune system that is suppressed as a result of malnutrition secrets the virus three times longer than does a child with normal nutrition.

Post-Measles Corneal Ulceration in Children in Northern Nigeria: The Role of Vitamin A, Malnutrition and Measles

M. Inua, M.B. Duggan, C.E. West, H.C. Whittle, O.I. Kogbe, J.H. Sandford-Smith and J. Glover. Ann Trop Paediatr 1983 Dec;3(4):181-91.

Authors' abstract: This work was prompted by the observation that corneal ulceration was apparently more common in young children in the guinea savannah area of northern Nigeria than in children in the tropical rainforest areas of southern Nigeria, where the intake of vitamin A, as the provitamin in red palm oil, is higher. Since corneal ulceration was usually seen in association with measles, a study was carried out to clarify the relationship between nutritional status, measles infection and vitamin A status in young children. The concentration of total retinol was measured in the plasma of well-nourished and malnourished children under three years of age, with or without a clinical record of recent measles. One hundred and twenty children were studied of whom 17 had corneal lesions. Malnutrition and measles were both found to depress the plasma concentrations of retinol and albumin. Measles depressed retinol levels (−20 to −30%) more than did malnutrition (−4 to −12%) while malnutrition had a greater depressing effect on albumin concentration (−23 to −30%) than did measles (−11 to −23%). The results support the hypothesis that corneal ulceration found in association with measles in northern Nigeria, although clinically similar to xerophthalmia, is not simply mediated through an effect of measles on the concentrations of vitamin A in plasma.

Liver Involvement in Measles Infection of Young Adults

M. Tishler and A.L. Abramov. Isr J Med Sci 1983 Sep;19(9):791-3.

Authors' abstract: Abnormal liver function was found in 34 (52%) of 67 young adults with measles; 5 of them (7%) also had a rise in bilirubin levels accompanied by icterus. Awareness of liver involvement in measles has been steadily increasing; consideration should be given to hepatitis as a possible complication of measles in young adults.

Hepatitis and Jaundice Associated with Measles in Young Adults. An Analysis of 65 Cases

D. Gavish, Y. Kleinman, A. Morag and T. Chajek-Shaul. Arch Intern Med 1983 Apr;143(4):674-7.

Authors' abstract: We analyzed the clinical course of 65 adult patients hospitalized because of measles during the years 1975 and 1981-1982. Liver involvement was found in 80% (52/65) of the patients, five patients had clinical jaundice. The disturbances of liver function tests reached their peak values between days 5 and 10 of the disease. In this study of measles in adulthood we have three observations of unusual interest: (1) hepatitis occurs commonly in the more severely ill patients and it may manifest clinically as jaundice; (2) long-term follow-up (up to seven years) shows a clear tendency to complete resolution of the liver damage; (3) there is a clear correlation between the severity of hepatic involvement and the occurrence of secondary bacterial infections.

Measles Virus-Specific IgM Antibodies in Sera from Patients with Chronic Active Hepatitis

K.E. Christie and G. Haukenes. J Med Virol 1983;12(4):267-72.

Authors' abstract: The occurrence of measles virus-specific IgM antibodies in sera from patients with chronic active hepatitis not caused by Hepatitis B virus was examined by a specific enzyme-linked immunosorbent assay (ELISA). Using whole serum, specific IgM antibodies were detected in 12 of 23 sera from patients with hepatitis B surface antigen (HBsAg)-negative chronic active hepatitis. In nine of these sera the finding of specific IgM antibodies was verified by separation of IgM by density gradient centrifugation and examination of the fractions by ELISA. Most of the sera from the patients with measles virus-specific IgM antibodies had an elevated level of specific IgG antibodies compared to the level of IgG found in control sera. The significance of these findings in view of a possible persistent measles virus antigen production in patients with chronic active hepatitis is discussed.

Late Morphologic Consequences of Measles: a Lethal and Debilitating Lung Disease Among the Poor

R.O. Kaschula, J. Druker and A. Kipps. Rev Infect Dis 1983 May-Jun;5(3):395-404.

Authors' abstract: Pneumonia that occurs within 28 days of the onset of measles rash is a common cause of severe pulmonary morbidity and/or death among poor children. The prevalence of such pneumonia can be related to the effectiveness of measles immunization programs. For 20 of 57 new cases of bronchiectasis in children undergoing bronchography, a strong causal relationship to measles was found. The lungs of 21 unselected children who died in the wake of measles were examined. Severe necrosis of bronchi and bronchioles was found in those children who had developed intercurrent adenovirus and herpesvirus infections. Bacterial suppuration produced a less severe necrosis. It is suggested that intercurrent adenovirus and herpesvirus infections that occur following measles are the most important initiating causes of follicular bronchiectasis in childhood. The severity of these supervening infections may be mediated by the transient immune suppression that occurs as a consequence of both measles and inadequate nutrition.

The Radiological Aspects of Chest Complication in Childhood Measles

A.I. Akamaguna and J.C. Odita. Ann Trop Paediatr 1982 Sep;2(3):129-32.

Authors' abstract: Chest radiographs of 335 Nigerian children presenting with pulmonary and cardiac complications of measles were studied systematically. Perihilar (88%) and diffuse (69%) pulmonary infiltrates were the commonest findings. Other abnormalities included segmental consolidation (34%), emphysema (20%), cardiomegaly (12%) and atelectasis (10%). Pneumothorax and pleural effusion were seen in 24 (7%) and 14 (4%) children, respectively. Eight children (2.5%) had subcutaneous and mediastinal emphysema. In patients with atelectasis and segmental consolidation there was a striking preponderance of right sided lesions.

Measles Encephalomyelitis—Clinical and Immunologic Studies

R.T. Johnson, D.E. Griffin, R.L. Hirsch, J.S. Wolinsky, S. Roedenbeck, I. Lindo de Soriano and A. Vaisberg. N Engl J Med 1984 Jan 19;310(3):137-41.

Authors' abstract: We studied 19 patients with postinfectious encephalomyelitis complicating natural measles-virus infections, and our results support the hypothesis that this demyelinating disease has a pathogenesis similar to that of experimental allergic encephalomyelitis. Early myelin destruction was demonstrated by the presence of myelin basic protein in cerebrospinal fluid, and lymphocyte proliferative responses to myelin basic protein were found in 8 of 17 patients tested. A lack of intrathecal synthesis of antibody against measles virus suggests that measles encephalomyelitis may not be dependent on virus replication within the central nervous system. Similar lymphoproliferative responses to myelin basic protein of lymphocytes from single patients with encephalomyelitis after rabies vaccine or after varicella or rubella virus infections suggest a common immune-mediated pathogenesis for the perivenular demyelinating disease that can follow the injection of neural tissues or infection by a variety of viruses.

Microtiter Determination of Measles Hemagglutination Inhibition Antibody with Filter Papers

J.H. Nakano, D.L. Miller, S.O. Foster and E.W. Brink. J Clin Microbiol 1983 May;17(5):860-3.

Authors' abstract: Epidemiological studies of measles and measles immunization frequently require determination of measles antibody status. In developing countries, where venipuncture is frequently unacceptable and where refrigerated storage of serum specimens is often unavailable, microtiter techniques not requiring refrigeration are required. We developed a filter paper technique that measures measles hemagglutination inhibition antibody and meets these criteria. Comparison of separately collected venous blood and peripheral blood collected on filter paper demonstrated 97% agreement in terms of presence or absence of antibody. In 30 of 32 measles specimens, 94% of titers were the same or varied by less than 2 twofold dilutions.

A Fourteen-Year Study to Identify Measles Antigen in Urine Specimens by Fluorescent-Antibody Methods

J.F. Boyd. J Infect 1983 Mar;6(2):163-70.

Author's abstract: Between 1965 and 1979 inclusive, 426 morning urine specimens from 410 patients admitted to hospital with the provisional diagnosis of measles were tested for measles antigen by fluorescent-antibody methods. One hundred and forty-two specimens (33.3 per cent) were positive. Of 74 patients who were clinically assessed not to have measles, 6/77 specimens (7.8 per cent) gave false positive results, and 71/77 (92.2 per cent) gave true negative results. Three hundred and forty-nine urine specimens were tested from 336 patients clinically judged to have had measles and 136 of these specimens (39 per cent) were positive. The positive rate was highest in a small number of specimens taken before the rash and next highest at the onset of the rash. The positive rate then fell; it rose again near the end of the first week, but the further increased positive rate after that time was associated with very small numbers of specimens. Of 12 child contacts of measles, 5/12 (41.67 per cent) had positive urine specimens and one of them

developed measles two days after sampling. None of the seven patients with negative urine specimens developed measles. Measles antigen was detected in urine sediment by fluorescent-antibody tests in 39 per cent of the patients with measles studied.

Cellular Immune Responses During Complicated and Uncomplicated Measles Virus Infections of Man

R.L. Hirsch, D.E. Griffin, R.T. Johnson, S.J. Cooper, I. Lindo de Soriano, S. Roedenbeck and A. Vaisberg. Clin Immunol Immunopathol 1984 Apr;31(1):1-12.

Authors' abstract: Lymphocytes from patients with measles showed profound and prolonged suppression of proliferative responses to mitogens. The degree of suppression was similar in patients with uncomplicated measles virus infection and in those with pneumonia or postinfectious encephalitis. Despite this suppression, lymphocyte responses to measles antigen and PPD were demonstrated in patients with encephalitis and uncomplicated disease, even early in infection. Most patients with pneumonia did not have demonstrable antigen-specific responses. The proportions of T helper (OKT 4) and T suppressor (OKT 8) cells and functional tests of Con A suppressor cell activity showed no significant difference between control and measles patients but, in contrast to controls, cells from measles patients cultured in the absence of any stimulant significantly suppressed the proliferation of allogeneic responder cells. Nine of 20 supernatant fluids from these cultures possessed a soluble suppressor factor. These studies indicate varied disruptions of immune reactivity during measles.

Epidemiology

Impact of Measles in the United States

A.R. Hinman, W.A. Orenstein, A.B. Bloch, K.J. Bart, D.L. Eddins, R.W. Amler and C.D. Kirby. Rev Infect Dis 1983 May-Jun;5(3):439-44.

Authors' abstract: Measles has had a severe impact on children in the United States since colonial times. In the early decades of the 20th century, thousands of fatal measles infections were reported each year. During the 1950s an annual average of greater than 500,000 cases of measles and nearly 500 deaths due to measles were reported in the United States. Surveys indicated that 95% of the population had been infected with measles by the age of 15 years. The introduction of measles vaccine and its widespread use, which began in 1963, has had a major impact on the occurrence of measles in the United States. Reported numbers of cases, deaths due to measles, and complications of measles (e.g., encephalitis) have declined dramatically. Accompanying the decline in reported incidence of measles and following it by approximately seven years, has been a decline in the reported incidence of subacute sclerosing panencephalitis (SSPE). In recent years, the incidence of measles has dropped to levels that are less than 1% of those seen in the prevaccine era. In 1981, provisional figures indicated that only 10% of counties in the United States reported any cases of measles. The reported incidence in 1981 was 1.3 cases per 100,000 population, compared with an average incidence of 336.3 cases per 100,000 population in the decade 1950-1959. Thus, the impact of measles in the United States has been markedly reduced, and it is anticipated that indigenous transmission will be eliminated entirely from the country within the year.

Impact of Measles in Canada

R.P. Larke. Rev Infect Dis 1983 May-Jun;5(3):445-51.

Author's abstract: The reported incidence of measles in Canada in 1981 was reduced 97% from the average annual rates during the prevaccine period, 1949-1958. Throughout recent years the age-specific incidence of reported cases of measles has remained highest in the group five to nine years of age, but there has been a definite increase in the proportion of cases of measles in persons greater than 10 years of age. During the extensive measles epidemic in Alberta in 1979, a high proportion of the reported cases occurred in adolescents and young adults previously vaccinated with killed vaccine, and the majority of these developed atypical measles syndrome. In Canada, from five to 36 patients per 100,000 population have required hospitalization annually for complications due to measles over the past 16 years. Measles-related deaths have declined in a pattern similar to that for reported incidence. Despite favorable trends in the control of measles in Canada, the social and economic impacts of this disease remain substantial and warrant a nationwide effort to eliminate indigenous infection.

Current Impact of Measles in the United Kingdom

C.L. Miller. Rev Infect Dis 1983 May-Jun;5(3):427-32.

Author's abstract: Annual measles notifications in the United Kingdom continue to exceed 100,000 despite the introduction in 1968 of routine measles vaccination for children aged one to two years. One in 5,000 children with notified cases of measles die; complications of the disease remain similar in incidence and severity to those observed in 1963. The overall vaccine acceptance of 50% has reduced notifications of disease primarily among children aged one to four and five to nine years. In areas where vaccination acceptance is higher than the national average, there has been a reduction in notifications for all age groups. Schwarz strain vaccine, which has been in use since 1968, has been shown to give protection lasting up to 16 years. Despite the reduction in the incidence of measles and the low acceptance of vaccine, no apparent increase has been found in the number of 11-year-old

children susceptible to measles, a finding demonstrated by an unchanging percentage of children with measles antibody from 1974-1981.

Impact of Measles in France

M. Rey, J. Celers, Y. Mouton and R. Netter. Rev Infect Dis 1983 May-Jun;5(3):433-8.

Authors' abstract: Although measles vaccine has been licensed since 1968, immunization against measles has not met with much success in France, partly because the disease is no longer feared. The level of vaccination coverage appears to be less than 20%. Indeed, the present epidemiologic situation is similar to the natural situation in a developed country. A multicenter, retrospective hospital survey revealed that 1,157 patients with measles were hospitalized during a 30-month period in five areas (total population, 4.2 million). Analysis of the preliminary results of this survey and of available national data showed an incidence of 5.6-7.5 cases per 1,000 population; a hospitalization rate of one per 10,000; a death rate of 0.56 per 1 million; and a disability rate of 0.48 per 1 million. Encephalitis (the definition of which should be reappraised) occurred once in 2,850 cases, and subacute sclerosing panencephalitis was not rare (incidence, one case per 2.6 million people). The problem posed by measles is sufficiently grave to justify a national campaign urging the widespread vaccination of children.

Measles Mortality and Vaccine Efficacy in Rural West Africa

H.F. Hull, P.J. Williams and F. Oldfield. Lancet 1983 Apr 30;1(8331):972-5.

Authors' abstract: Measles mortality and measles vaccine efficacy were determined during outbreaks in three Gambian villages. There were 146 cases of measles among 1073 children younger than 11 years. Thirty per cent of the children had been vaccinated against measles. The attack rate in unvaccinated children aged 9-47 months was 43% compared with 6% for children of the same age with documented measles vaccination. Vaccine efficacy was 37% for children vaccinated at 6-8 months of age and 89% for children vaccinated at 9 months or older. Five per cent of measles cases died before the initial investigation of the outbreaks and a further 10% of cases died during the ensuing 9 months. Only 1% of children who did not contract measles died in the 9 months after the outbreaks. Case-fatality rates were highest for measles patients less than 1 year old (64%) and fell with age. Measles remains a significant source of acute and delayed mortality in unvaccinated African populations.

Measles Mortality, State of Nutrition, and Family Structure: A Community Study from Guinea-Bissau

P. Aaby, J. Bukh, I.M. Lisse and A.J. Smits. J Infect Dis 1983 Apr;147(4):693-701.

Authors' abstract: In an urban area of Guinea-Bissau where the general state of nutrition seemed fairly good, the case fatality rate for measles among children less than three years of age who were examined clinically during an epidemic was 25.0%. Nutritional indicators (weight-for-age, height-for-age, and weight-for-height ratios) measured a few months before the epidemic were about equal both for the group of 60 children who subsequently died of measles and for the general child population. Because no community study has demonstrated that the nutritional state influences the outcome of measles, the assumed importance of the state of nutrition for measles fatality rates is questioned. Children in monogamous households had a lower risk of dying of measles. It is suggested that measles may be more severe in polygamous families because several children can have the disease simultaneously.

Measles Mortality and Malnutrition (Editorial)

Anonymous. Lancet 1983 Sep 17;2(8351):661.

From author's discussion: The high fatality and complication rates [of measles] of Europe in the distant past have been attributed to malnutrition and so has present-day experience in the developing world, but not everyone takes this view. Mortality rates of 20% or more accompany the combined effects of viral and secondary bacterial infections, resulting in severe prodromal symptoms, widespread confluent rash, and involvement of the respiratory and central nervous systems. Severe protein energy malnutrition (PEM) of the marasmic, kwashiorkor, or mixed type is almost invariably present under these circumstances, but to what extent it is causal or is a result of the infection is unclear.

Cell-mediated immunity is impaired during measles. Many aspects of immunity, especially of the cell mediated type, are also impaired in PEM and in deficiency of vitamin A and other nutrients, but it has not been demonstrated that immunosuppression is uniformly greater in malnourished children with measles than in those who are well nourished.

During a measles epidemic in Guinea-Bissau a high case fatality rate of 25% was found to be unrelated to nutritional status, as assessed by anthropometric indices, but to be positively correlated with family size. While this study draws attention to the importance of exposure it does not rule out a role for malnutrition in survival since the nutritional status was assessed several months before the epidemic and was in general good.

Data collected from urban, periurban, and rural locations in Natal/Kwa Zulu in South Africa showed a positive correlation between population density and percentage of measles cases aged 8 months or less, ...emphasizing the need for protection of the very young against measles, especially in high-density regions. Many studies have shown that measles mortality is highest in children under 1 year in the lowest socioeconomic groups. It may be relevant that marasmus, the most prevalent form of severe PEM, has its peak incidence in these early months of life.

Age at and Time Since Vaccination During a Measles Outbreak in a Rural Community

H.S. Faust and F.E. Thompson. Am J Dis Child 1983 Oct;137(10):977-80.

Authors' abstract: During winter 1978, 350 cases of measles were reported in Livingston County, Michigan, a small, rural county. Of these cases, 250 occurred in the school-aged population. A search of school records and contact with parents provided complete vaccination data on 5,973 students. Attack rates in children vaccinated at the age of 12 months or younger were more than twice the rates of those vaccinated at older ages. Time since vaccination was not a statistically significant predictor using multiple logistic analysis.

Measles on Campus

R.W. Amler, R.J. Kim-Farley, W.A. Orenstein, S.W. Doster and K.J. Bart. J Am Coll Health 1983 Oct;32(2):53-7.

Authors' abstract: The lack of immunization requirements at the nation's colleges and universities threatens the maintenance of the interruption of indigenous measles in the United States. The high susceptibility rates in some college populations coupled with the high mobility of college students who may travel to countries where measles is endemic or epidemic increases the potential for measles outbreaks.

Preventing measles in college-age populations is particularly important because the disease can be more serious in adults. In view of the importance of preventing measles in college students, the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service has recommended that officials strongly consider immunization requirements for college entry.

The ultimate goal of rubella immunization is the protection of a future fetus against damage from intrauterine infection. Although rubella cases are reported routinely on college campuses, most colleges make no effort at controlling these outbreaks or instituting immunization requirements. The ACIP strongly urges educational institutions to require proof of immunity to rubella for registration or employment.

Measles in England and Wales—III: Assessing Published Predictions of the Impact of Vaccination on Incidence

P.E. Fine and J.A. Clarkson. Int J Epidemiol 1983 Sep;12(3):332-9.

Authors' abstract: Published predictions of the impact which different levels of vaccination should have on measles incidence are discussed in the context of observed data on vaccine uptake and measles incidence in England and Wales. Discrepancies are noted between prediction and observation with regard to the effect of vaccination on epidemic periodicity, epidemic size, age distribution of cases, and the disappearance of measles from communities. These errors are attributable to failures to recognize the implications of seasonal trends in incidence, age dependence of risk, and the non-homogeneity of human populations. Predictive models are useful hypotheses, but should be assessed critically against observation.

Prevention and Control

Elimination of Indigenous Measles from the United States

A.R. Hinman, C.D. Kirby, D.L. Eddins, W.A. Orenstein, R.H. Bernier, P.M. Turner and K.J. Bart. Rev Infect Dis 1983 May-Jun;5(3):538-45.

Authors' abstract: In October 1978, a nationwide initiative to eliminate indigenous measles from the United States by October 1, 1982, was announced. The measles elimination program has three major elements: attaining and maintaining high immunization levels, aggressive and effective surveillance, and vigorous response to cases. In 1980, immunization levels in children entering school for the first time were 96%, indicating that the necessary levels have been attained in the age group. Mechanisms are in place to assure maintenance of these levels; these rely heavily on the use of immunization requirements for school attendance in each state. Aggressive surveillance systems have been developed for each state to detect suspected measles cases as soon as possible after they occur and to investigate them within 24 hours of notification. The clinical definition of measles used is fever of $\geq$101 F (38.3 C); rash of three or more days duration; and cough, coryza, or conjunctivitis. The response to outbreaks involves identifying persons in the area who are at risk of contracting measles, determining those who are possibly susceptible, and ensuring that these persons are vaccinated. In school outbreaks, susceptible students are vaccinated or excluded from school until the outbreak is over. During 1981, measles morbidity reached a record low level of only 3,032 reported cases (provisional total). Epidemic measles occurred in only a few outbreaks of

limited size and duration, and endemic cases were restricted to a small number. Imported cases averaged slightly more than two per week, occasionally producing limited outbreaks, but more often resulting in no secondary spread. Transmission of measles has been interrupted in most of the United States. With continued vigorous implementation of the current strategy and with additional measures to lessen the risk of importations, it appears likely that the goal to eliminate indigenous measles transmission will be attained by October 1982.

Measles and Rubella: Our Remaining Responsibilities (Editorial)

S.W. Doster, H.C. Stetler, W.A. Orenstein, K.J. Bart and A.R. Hinman. Am J Public Health 1983 May;73(5):490-2.

Authors' abstract: Extraordinary progress has been made toward eliminating the transmission of indigenous measles in the U.S. There are, however, three areas of concern which threaten the maintenance of the interruption of indigenous measles transmission in the U.S.: (1) the continuing threat that imported measles cases might reestablish transmission; (2) whether the number of susceptibles caused by the 3-8 per cent primary vaccine failure rate will accumulate and be able to sustain transmission following a reintroduction of measles; and (3) that, in the absence of disease, interest in maintaining high immunization levels will wane allowing accumulation of susceptibles and the reestablishment of transmission.

Progress also has been made in the reduction of the incidence of rubella. However, 10 to 20 per cent of adolescent and young adults remain susceptible. Earlier fears that rubella vaccine virus might be teratogenic have not been substantiated. These findings indicate that rubella vaccination should be actively encouraged in adolescents and young adults.

Measles and Rubella on College Campuses: The Need to Act

K.J. Bart and D.H. Stenhouse. J Am Coll Health 1983 Oct;32(2):58-62.

Authors' abstract: The lack of immunization requirements at the nation's colleges and universities threatens the maintenance of the interruption of indigenous measles in the United States. The high susceptibility rates in some college populations coupled with the high mobility of college students who may travel to countries where measles is endemic or epidemic increases the potential for measles outbreaks.

Preventing measles in college-age populations is particularly important because the disease can be more serious in adults. In view of the importance of preventing measles in college students, the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service has recommended that officials strongly consider immunization requirements for college entry.

The ultimate goal of rubella immunization is the protection of a future fetus against damage from intrauterine infection. Although rubella cases are reported routinely on college campuses, most colleges make no effort at controlling these outbreaks or instituting immunization requirements. The ACIP strongly urges educational institutions to require proof of immunity to rubella for registration or employment.

International Symposium on Measles Immunization: Summary and Recommendations

S.L. Katz. Pediatrics 1983 Apr;71(4):653-4.

Author's abstract: Throughout the world there remains great variation in morbidity and mortality due to measles, in the extent of vaccine utilization, and in attitudes about measles as a serious health problem. Measles vaccines have proven to be safe and immunogenic; aerosol administration of the vaccine merits further study. Motivational issues, especially in developed countries, and technologic issues, especially in developing nations, are very important. Clinical and laboratory surveillance have their appropriate uses in assessing program success. A one-dose schedule, administered to an infant after one year of age, seems preferable; booster doses or immunization before the first year should be considered in special situations. Other issues of importance are management of individuals previously vaccinated with inactivated vaccine; use of educational and motivational materials; the problem of measles importations from other countries; and the eventual worldwide eradication of measles.

Policy for Measles Elimination in Canada and Program Implications

F.M. White. Rev Infect Dis 1983 May-Jun;5(3):577-82.

Author's abstract: In Canada, both the National Advisory Committee on Immunization and the Canadian Pediatric Society have recommended a goal of measles elimination. Because immunization services are a responsibility of the provincial government, most provinces maintain advisory bodies to respond more specifically to their needs and to interpret national recommendations within the provincial context. Provincial responses to the measles elimination proposal are reviewed with reference to legislation and to components of the feasibility of the program, such as financial support, levels of staffing, efficacy of vaccine, surveillance, management of records, handling of vaccine, security of supply, type of delivery system, and desirability of a federal financial commitment. Clarification of national recommendations is urged, especially with regard to revaccination of individuals who previously received killed measles vaccine. Progress in provincial programs is reviewed, and a flexible approach is advocated in view of the different epidemiologic circumstances and delivery systems among the provinces.

If adopted by all Canadian provinces, the goal of measles elimination within the current decade may be feasible for North America.

Measles Control in the United Kingdom

T.M. Pollock. Rev Infect Dis 1983 May-Jun;5(3):574-6.

Author's abstract: In the United Kingdom measles vaccine is known to be highly effective, but only half of the children of eligible age are vaccinated. Many doctors are doubtful about the risks and benefits of measles vaccination. Although serious reactions are rare, convulsions occur in one per 1,000 children vaccinated in England, and malaise after vaccination is common. Insufficient effort seems to have been made to convince family doctors of the undoubted value of the vaccine. In the few areas where motivation is high, good vaccination rates have been achieved. The introduction of measles vaccination 14 years ago has markedly reduced disease incidence to approximately 75% of the preimmunization level. So far regular surveys have not suggested any tendency for the proportion of susceptible individuals among the older population to increase.

Epidemiology and Specific Prophylaxis of Measles

T.V. Peradze and A.A. Smorodintsev. Rev Infect Dis 1983 May-Jun;5(3):487-90.

Authors' abstract: In studies in the USSR, a single dose of Leningrad-16 live measles vaccine induced seroconversion in at least 90% of vaccinees, with a mean titer of serum antibody of 1:32 and high antibody levels throughout the 15 years after vaccination. When the vaccine was correctly stored, transported, and used for mass vaccination, measles-associated morbidity decreased and the circulation of measles virus was interrupted in some towns for several years. However, childhood vaccination over a long period changed the immunologic age of the population and resulted in increased measles-associated morbidity in adults. A program for eradication of measles virus in some areas of the USSR has thus been developed. The ultimate aim of this program is the total eradication of measles. This goal can be achieved only after attainment of a high level of collective immunity (95%) through increased efficacy and quality of the vaccine. The international program of measles eradication should be based on the experiences gained through immunization programs in various countries. The key issues are (1) the elimination of measles epidemics and mortality, (2) the maintenance of a low incidence of measles over a long period, (3) the prevention of measles virus importation through epidemiologic surveillance, and (4) the maintenance of a high level of collective immunity in the total population.

Evolution of the Measles Vaccination Program in Costa Rica

E.M. Leon de Coto. Rev Infect Dis 1983 May-Jun;5(3) 588-91.

Author's abstract: The vaccination program instituted in Costa Rica in 1967 has had a great impact on measles. Since 1973 the downturn in measles morbidity and mortality are due solely to the continued vaccination of susceptible children throughout the country. An epidemic outbreak occurred in 1977. Since the vaccine was given primarily to children of school age, this outbreak probably was the result of an accumulation of susceptible subjects. There was little change in the mortality rates. Programs resulting in a coverage of 70% attempted to prevent a new outbreak in 1979, but failed. Because the vaccine was routinely administered to children one year of age and older, most of the cases were in the group younger than that age. At present, the incidence of measles is minimal, and no fatalities occurred in 1981. Vaccination coverage for children two years of age exceeds 90%, and Costa Rica's goal is the complete eradication of the disease.

Control of Measles in Czechoslovakia (CSSR)

J. Sejda. Rev Infect Dis 1983 May-Jun;5(3):564-7.

Author's abstract: Mass immunization against measles in the Czechoslovak Socialist Republic (CSSR) began in 1969 and utilized the Czechoslovak vaccine, which corresponds in its parameters to the further-attenuated measles vaccines. The immunization rate for relevant age groups of the population (i.e., children born in 1968-1980) is already 98%-99% in 1982. Measles morbidity decreased to less than 2% of the incidence before the introduction of immunization, and mortality now is practically negligible. The decade 1972-1982 produced significant changes in epidemiologic characteristics of measles. Of importance is the gradual shift in the age distribution of affected children to older, nonimmunized age groups. Results of yearly immunologic surveys of a broad, randomly selected population sample have become the decisive criteria for evaluation of vaccine efficacy. The program of revaccination of all children was chosen as the optimal strategy for maintaining measles elimination. This program aims at ensuring a level of herd immunity in the whole population of $\geq 95\%$.

Introduction to the Control of Measles by Vaccination in the People's Republic of China

Y. Zhiang and W. Su. Rev Infect Dis 1983 May-Jun;5(3):568-73.

Authors' abstract: Measles vaccine is provided free of charge in China. In big cities the section clinics are responsible for measles vaccination. In rural areas, barefoot doctors go from door to door to administer the vaccine, or parents are told to bring their children to the coopera-

tive medical station for vaccination. In most parts of China, eight months is considered the optimal age for primary vaccination. The seroconversion rates are usually greater than 90%. With the elapse of time, titers of hemagglutination-inhibiting antibody decreased regularly and even declined to an undetectable level. As a result some people who had been vaccinated became ill with measles. Thus, one vaccination cannot guarantee persistence of antibody for life. It would be appropriate to carry out revaccination for maintenance of adequate immunity against measles. In view of the situation in China as a developing country, the main goal of the campaign against measles in the near future should be the broadening of effective vaccination coverage for control of epidemics, the reduction in incidence, and the lowering of the fatality rate. Measles can definitely be eliminated as has already been done for smallpox.

Selective Primary Health Care: Strategies for Control of Disease in the Developing World. IV. Measles

J.A. Walsh. Rev Infect Dis 1983 Mar-Apr;5(2):330-40.

Author's abstract: Measles, a highly contagious viral disease, kills several hundred thousand infants and young children yearly. Essentially all children will become infected; at least 1% of those living in developing countries will die unless protected by immunization. In urban areas, peak incidence occurs in those younger than three years. The youngest and most undernourished children suffer the most severe complications and the highest risk of death. Diarrhea, malnutrition, pneumonia, and blindness associated with vitamin A deficiency are the worst complications. The infection is preventable by the timely administration of a potent vaccine. This endeavor requires a well-managed technical and administrative network that remains difficult to organize in many areas of the world. The vaccine is efficacious and has few adverse effects but must be provided to children during the short interval between loss of transplacentally acquired antibodies and the acquisition of natural infection. The improvements in heat stability of the vaccine increase the likelihood of providing potent vaccine, but a well-managed cold chain remains a prerequisite for any successful immunization program. Health education, improved management skills, publicity, and community support are all important factors for ultimately preventing the morbidity and mortality from this disease.

Measles and Models (Editorial)

K.J. Bart, W.A. Orenstein, A.R.Hinman and R.W. Amler. Int J Epidemiol 1983 Sep;12(3):263-6.

Authors' abstract: Mathematical models played a role in the development of strategies for the first successful measles elimination program which started in 1966 as part of a program of smallpox eradication and measles control in West Africa and in the inception of the measles eradication program in the United States.

Mathematical models have been developed to describe outbreaks, to test concepts, and to provide insights into disease control and policy formulation. The resulting equations sometimes mirror the described events, but to date, have had little impact upon disease control or preventive practices. Instead they have been used retrospectively to reassure rather than assist in the development of policy. Mathematical models serve to clarify the targets, but do not provide the political will.

Measles could and should be eliminated in Europe where 800 deaths a year occur due to measles. In many developing countries the magnitude of the problem posed by measles is well recognized and there is a major impetus to try to introduce measles vaccine and expand its coverage.

Substantial impediments to global measles control still exist: technical, epidemiological, economic, and political. Only if it can be convincingly demonstrated that measles can be eliminated in countries where elimination has been undertaken will other developed nations follow the lead and only if they join in will the necessary international economic and political support be given to the developing world to help carry out the global task.

Measles Immunization: Remaining Needs for Research

W.S. Jordan, Jr. Rev Infect Dis 1983 May-Jun;5(3): 613-8.

Author's abstract: Highly immunogenic, safe, and effective attenuated measles vaccines, stabilized to lengthen duration of potency under field conditions, are available. Measles can be controlled while studies continue to define the molecular change in the viral genome responsible for attenuation and to clone the genes that specify for the two major surface glycoprotein antigens, the hemagglutinin (HA) and fusion (F) proteins. Purification of HA and F antigens will facilitate studies of cell-mediated immunity. Elucidation of host cell-dependent lack of synthesis of the internal membrane protein in the brains of patients with subacute sclerosing panencephalitis (SSPE) is needed. Control of measles will clarify the relationship between acute measles and those chronic neurologic diseases known (e.g., SSPE) or thought (e.g., multiple sclerosis) to be caused by persistent infection with measles virus. Epidemiologic studies should determine the optimal age for immunization as age-specific morbidity and mortality are reduced and should record the subsequent course of apparent vaccine failures in children immunized from seven to 15 months of age. Behavioral and operational research must examine how best to extend measles immunization throughout the world.

Further-Attenuated Measles Vaccine: Characteristics and Use

S. Krugman. Rev Infect Dis 1983 May-Jun;5(3):477-81.

Author's abstract: Further-attenuated strains of measles virus may be distinguished from virulent strains by the following characteristics. Unlike virulent strains, attenuated strains of measles virus can be propagated in chick embryo fibroblast cultures, induce production of interferon in tissue culture cells, and produce plaques that can be distinguished from those produced by virulent strains. Unlike virulent measles virus, attenuated strains induce an inapparent infection in approximately 85% of vaccinees. Symptoms such as fever, cough and rash, if present, are usually transient. Bacterial and central nervous system complications associated with natural measles infection are extremely rare after immunization. A 16-year, prospective study of immunologic response of 47 children who had natural measles and of 70 children immunized with live, further-attenuated measles vaccine revealed (1) that all 47 children with natural measles infection had high titers of hemagglutination-inhibiting (HAI) antibody (≥1:64) one month after vaccination and 15% had low titers (1:2-1:4) 16 years after vaccination; and (2) that all 70 children who received live, further-attenuated measles vaccine had high titers of HAI antibody (≥1:64) one month after vaccination, but in 36% of the group the titers declined to less than 1:8 16 years later. Neutralizing antibody was detectable in convalescent sera that had lost detectable HAI antibody. Reimmunization of children with undetectable HAI antibody induced a classic booster response. These prospective immunologic studies confirmed that immunity persists after immunization as well as after natural measles infection.

Stability of Further-Attenuated Measles Vaccines

G.F. Mann, L.M. Allison, J.S. Lloyd, P. Tam, A.J. Zuckerman and F.T. Perkins. Rev Infect Dis 1983 May-Jun;5(3):482-6.

Authors' abstract: Accelerated stability tests on lyophilized measles vaccines show two distinct mechanisms of virus inactivation. A rapid initial loss of infectivity occurs only on exposure to temperatures above the ambient temperature. This loss is temperature related and may be attributable to the movement of residual moisture from the virus pellet into the void space of the vial. Subsequent inactivation of virus occurs at all temperatures as a first-order reaction that follows Arrhenius kinetics. Integration of values for these two components allows precise prediction of vaccine stability at any temperature. Analysis of the results obtained for greater than 30 vaccines shows that those which are stable for one week at 37 C have a predicted life of more than one year at 8 C. This simple test is now being applied to the identification of unstable products. The rate of this reaction is closely, if conservatively, matched by a time-temperature color indicator, which may be useful for monitoring vaccine quality.

Measles Vaccines Used in Japan

M. Hirayama. Rev Infect Dis 1983 May-Jun;5(3):495-503.

Author's abstract: The history of the research and development of measles vaccines is described and the efficacy of and adverse reactions to the Japanese licensed vaccines are discussed. The 10-year follow-up studies revealed that the incidence of clinical measles was 11.5% among those inoculated with live vaccines in combination with killed vaccines, whereas it was only 1.9% among those given live vaccines attenuated to the level of the Schwarz vaccine. Use of the Schwarz and Biken-CAM vaccines resulted in satisfactory antibody responses in ≥97% of vaccinees. However, these vaccines caused a febrile reaction of ≥37.5 C in 50% of vaccinees and one of ≥39 C in 15% of vaccinees. On the other hand, a febrile reaction was observed in 20% and 5%, respectively, of children immunized with the AIK-C vaccine or the further-attenuated Schwarz vaccine, both of which were developed in Japan. The worldwide use of further-attenuated vaccines is strongly recommended. The system of fixed surveillance stations, which was started in 1981 by the Japanese government with the voluntary cooperation of pediatricians and ophthalmologists, is described. This system proved effective in obtaining information about the prevalence of communicable diseases, including measles, in childhood and about the efficacy of vaccines.

Response to Live Attenuated Measles Vaccine in Children with Severe Kwashiorkor

G.M. Powell. Ann Trop Paediatr 1982 Sep;2(3):143-5.

Author's abstract: An impaired response to vaccination with live attenuated measles vaccine was found in severely malnourished children, when compared with well nourished controls. It is suggested that humoral immune response may fail in children with severe protein energy malnutrition due to diversion of available amino acids to other uses. The possibility of a delayed antibody response to measles vaccine in malnourished children was not excluded.

Measles Antibody Levels From Birth to 9 Months of Age in Nigerian Infants

M.B. Abdurrahman, B.M. Greenwood, O. Olafimihan and H.C. Whitle. Afr J Med Med Sci 1982 Sep;11(3):113-5.

Authors' abstract: Measles antibody (HAI) titers were measured in healthy Nigerian infants at birth and at 3, 6 and 9 months of age. At birth only one baby out of thirty-five had HAI titer of less than 1:4, but at 3 months of age

titers had fallen to this level in 33% of children. The percentage increased further to 78.6% at 6 months of age. At 9 months, nine out of twenty-seven (33%) infants had HAI titer of 1:16 and above, suggesting recent measles infection or immunization. The rapid fall in HAI titers up to 6 months could explain the occurrence of measles in early age in tropical countries. We recommend that children in Nigeria be immunized at 7-8 months of age.

The Optimal Age for Vaccination Against Measles in an Asiatic city, Taipei, Taiwan: Reduction of Vaccine Induced Titer by Residual Transplacental Antibody

Y.L. Lee, F.L. Black, C.L. Chen, C.L. Wu and L.L. Berman. Int J Epidemiol 1983 Sep;12(3):340-3.

Authors' abstract: Children vaccinated when aged between six and thirteen months against measles in Taipei showed a high frequency of response, similar to that reported from Nairobi, Kenya and contrasting with analogous data for the USA. The age for optimal protection against measles mortality by a single dose of vaccine in this group of children is nine months. Maternal antibody exerted a negative effect on measles antibody titer in vaccinees beyond the age at which it blocked the response so that the infants of mothers with the higher titers themselves had lower titers. A separate effect of immunological immaturity on titer of the response could not be demonstrated in children over six months of age.

Age-Specific Occurrence Rates of Measles in Urban, Peri-Urban, and Rural Environments: Implications for Time of Vaccination

W.E. Loening and H.M. Coovadia. Lancet 1983 Aug 6;2(8345):324-6.

Authors' abstract: Measles vaccination is unsatisfactory in infants less than 8 months old. To find out what proportion of children with measles in the developing world fall within this age range, a survey was conducted in Natal/Kwa Zulu. Data were collected from urban (community-based survey, infectious diseases hospital data, referral center date), peri-urban (regional hospital and clinics), and rural (3 local hospitals and their peripheral clinics) populations. There was a positive association between population density and the percentage of measles cases aged 8 months or less. 20-45% of measles patients in urban areas, 15% in the peri-urban zone, and 6-12% in rural Kwa Zulu had the disease at or below 8 months of age. The mortality rate for measles in this age group at the referral center was 26%. There is an urgent need for effective methods of immunizing the very young against measles in high-density regions of developing countries.

Risk of Pregnancy Among Adolescent Schoolgirls Participating in a Measles Mass Immunization Program

J.M. Mann, J.M. Montes, H.F. Hull, N. Greenberg, N. Kalishman, A.E. Pressman, S.G. Kennedy and C.T. Iddings. Am J Public Health 1983 May;73(5):527-9.

Authors' abstract: A large measles vaccination program in the Albuquerque, New Mexico public schools in 1981, conducted according to U.S. Public Health Service guidelines, was studied to determine rates of pregnancy among adolescent vaccinees. Pre-vaccination counseling of 1,922 clinic attendees prevented seven pregnant girls from being vaccinated. Despite counseling, of 1,913 female vaccinees age 13-18 years old, two were pregnant at the time of vaccination (1.05 pregnancies per 1,000 vaccinees) and an additional four girls became pregnant in the three months after vaccination (2.1 pregnancies per 1,000 vaccinees). Data supporting low or absent fetal risks from measles and rubella vaccine, combined with the low pregnancy rate among vaccinees documented in this study, support the reasonableness of the recommended strategy for measles and rubella vaccination of secondary schoolgirls.

Successful Immunization of Children With and Without Maternal Antibody by Aerosolized Measles Vaccine. I. Different Results with Undiluted Human Diploid Cell and Chick Embryo Fibroblast Vaccines

A.B. Sabin, A. Flores Arechiga, J. Fernandez de Castro, J.L. Sever, D.L. Madden, I. Shekarchi and P. Albrecht. JAMA 1983 May 20;249(19):2651-62.

Authors' abstract: Inhalation of undiluted, aerosolized measles vaccine was immunogenic in 100% of 4- to 6-month-old and older children with and without residual maternal antibody when the human diploid cell (HDC) vaccine containing the Ikic (Edmonston-Zagreb) strain and 1% human albumin was used but in a smaller percentage of infants given a chick embryo fibroblast (CEF) vaccine, which contained the Edmonston-Schwarz strain, ten times more virus, and hypertonic sugar solution but no added protein. Prevaccination residual placentally transmitted plaque-neutralizing antibody titers of 25 to 512 that can prevent an immune response after subcutaneous injection of measles vaccine did not prevent an immune response after inhalation of aerosolized vaccine. There were no immediate clinical reactions in the 160 children who inhaled the aerosolized vaccines, and no significant subsequent reactions among the 96 children who were successfully immunized. There were no contact infections.

Immunization Against Measles by Aerosol

A.B. Sabin. Rev Infect Dis 1983 May-Jun;5(3):514-23.

Author's abstract: About 20 years ago, Japanese and American investigators found that inhalation of relatively small amounts of aerosolized, partly attenuated measles vaccines was consistently immunogenic in nearly all susceptible children. The resulting modified measles was not transmissible to susceptible children. In 1965-1966, Japanese investigators showed that levels of neutralizing antibody produced by killed measles virus vaccine, which prevented subsequent immunization when live vaccine was given subcutaneously, did not prevent the immunogenic effect of the same vaccine given by aerosol. This raised the possibility that aerosolized vaccine may be immunogenic in infants with residual maternal antibody, in whom subcutaneously injected vaccine is ineffective. In 1971, Soviet investigators reported the high effectiveness and complete lack of febrile and other clinical reactions in 3,306 children who were exposed in large groups in large tents or chambers to aerosols of the more-attenuated measles vaccines that were currently available. An inexpensive nebulizer and the procedure for administration of aerosolized vaccine to individual children are here described. If the good results reported from the USSR can also be obtained with this simple method of vaccination by aerosol, it may be possible to carry out mass vaccinations against measles with thousands of nonprofessional personnel and thereby quickly eliminate measles in countries where it is still a serious public health problem.

Aerosolized Measles Vaccine—Will It Open the Window? (Editorial)

R.W. Amler, W.A. Orenstein and K.J. Bart. Rev Infect Dis 1983 May-Jun;5(3):524-6.

Authors' abstract: Because the risks of severe complications and death from measles are highest for infants from 6 to 12 months of age in developing countries, measles vaccine must be targeted for a narrow "window" of age limits during which effective immunization can be accomplished before natural infection occurs. This narrow window is a barrier to successful disease control. Preliminary data suggest that aerosol measles vaccine (AMV) might "open the window" and permit vaccination of younger infants. More data are needed to evaluate the safety of AMV, though the observed risk of neurologic reactions to respiratory mucosal vaccination is zero (of over 3,000 vaccinees).

Before AMV can be incorporated into worldwide immunization strategies, more information is needed about its safety, cost, ease of administration to large groups of infants, and its stability in tropical climates. Nevertheless, AMV may help minimize the worldwide impact of measles if it is immunogenic in infants 4-6 months of age. Such an "open window" would give immunization programs a longer period during which to vaccinate children before they were at risk of natural disease.

Control of Measles by Annual Pulse Immunization

T.J. John, M. Ray and M.C. Steinhoff. Am J Dis Child 1984 Mar;138(3):299-300.

Authors' abstract: In a village with a population of more than 2,000, with measles outbreaks in alternate years, annual single-day measles immunization campaigns were conducted during four winter seasons. Measles vaccine was offered to children 1 year of age and older, with no previous measles or immunization. There has been no outbreak of measles since the introduction of immunization to date. Four cases of introduced measles did not result in any secondary cases. This vaccine delivery strategy (annual pulse immunization), designed to improve coverage and simplify cold chain management, was shown to be suitable for the control of measles in rural communities in the Third World.

Public Health Policy Toward Atypical Measles Syndrome in the United States

A.R. Hinman and J.P. Koplan. Med Decis Making 1982;2(1):71-7.

Authors' abstract: We used a Delphi Survey to obtain expert estimates of the risk of atypical measles syndrome (AMS) and other probabilities in order to estimate the magnitude of AMS as a public health hazard in the United States and thus guide policy formulation on control activities. The surveyed experts estimated that we might expect slightly more than 5,300 cases of AMS to occur in the future. Assuming all of these cases would occur over the next 20 years, we estimate the costs to society of these cases at $1.17 million. Costs of possible mechanisms for the control or prevention of these cases of AMS were considered. We conclude that the estimated future morbidity, mortality, and costs do not warrant a major health initiative. Rather, continued efforts should be made to ensure maintenance of physician awareness of the inefficacy of killed measles vaccine (KMV) and the need for revaccination of KMV recipients with live measles vaccine.

Severe Local Reactions to Live Measles Virus Vaccine Following an Immunization Program

H.C. Stetler, R.D. Gens and G.R. Seastrom. Am J Public Health 1983 Aug;73(8):899-900.

Authors' abstract: A cluster of nine severe local reactions occurred in a Pennsylvania school district following a mass measles immunization program in February 1981. A case-control study showed that the nine cases had a statistically significant increased history of having received killed measles vaccine previously ($p < .001$, Fisher's exact test) and a statistically significant higher geometric mean measles antibody titer ($p < .01$, Student's

t test) than controls, suggesting that previous receipt of killed measles vaccine was the underlying cause of these reactions.

Early-Onset Reaction After Measles Vaccination. Further Australian Reports

J. McEwen. Med J Aust 1983 Nov 12;2(10):503-5.

Author's abstract: Fifteen reports of reactions occurring within 30 minutes of vaccination with live attenuated measles virus have been received by the Adverse Drug Reactions Advisory Committee (ADRAC) up to March 30, 1982. These reactions were similar to those in three episodes reported recently. An acute change in skin color, described as cyanosis, slight cyanosis, or mottling was the most commonly reported symptom. All the children recovered. The causes and mechanisms of these reactions remain unknown.

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RUBELLA

General

Surveillance of Congenital Rubella and the Immunity Status to Rubella in the Jerusalem Area

M. Isacsohn, B. Rudensky, A.I. Eidelman, E. Paz, G. Weintraub, N. Nubani and T.A. Swartz. Isr J Med Sci 1983 Oct;19(10):929-33.

Authors' abstract: A retrospective study on the incidence of congenital rubella (CR) in the past 10 years in the Jerusalem area was conducted. After the 1972 epidemic, which resulted in 48 cases of congenital rubella, few sporadic cases of CR appeared each year, and in the 1978-1979 period the number of CR cases was relatively small. Immunity to rubella in different categories of population (children 3 months to 18 years, college students, nurses in pediatric, newborn and intensive care units, student nurses, and women of childbearing age) was determined by hemolysis in gel (HIG) and hemagglutination inhibition (HI) methods. Susceptibility was defined as an absence of antibody at a dilution of 1:16 in HI, and hemolysis of less than 7 mm in the HIG test. Compared with previous studies on the incidence of antibodies to rubella in women of childbearing age, a mild decrease in the percentage of seronegative women was found.

Clinical and Laboratory

Rubella and Congenital Cataracts (French)

J. Celers, M. Aymard, J. Feingold and D. Godde-Jolly. Arch Fr Pediatr 1983 May;40(5):391-5.

English summary: Between April 3, 1977 and June 6, 1980, 97 children with congenital cataracts and 97 evenly matched control children were examined in order to clarify the biological criteria of congenital rubella and to estimate its importance in the etiology of congenital cataracts. Although the age limit had been fixed at 60 months, the 1978 rubella outbreak accelerated immunization in young children and resulted in difficulties in interpreting some results. All children presenting with congenital cataracts associated with clinical symptoms of rubella embryopathy displayed anti-rubella antibodies including anti-rubella IgM up to the 13th month: they represent 16% of cases with congenital cataracts in this series. A rubella etiology could not be proven in children with clinically isolated congenital cataracts.

Outcome of Rubella During Pregnancy with Special Reference to the 17th-24th Weeks of Gestation

L. Grillner, M. Forsgren, B. Barr, M. Bottiger, L. Danielsson and C. De Verdier. Scand J Infect Dis 1983;15(4):321-5.

Authors' abstract: The consequences of rubella during pregnancy were studied with special reference to infections occurring during the 17th to 24th weeks of gestation. Laboratory confirmed rubella infected pregnancies were followed and the infants were examined clinically and serologically at a mean age of 20 months. In addition, children born to mothers with verified rubella in earlier epidemics were examined clinically at the age of 4 or 7 years. 491 cases of rubella in pregnant women from 1978-1980 were reported and 118 children were followed up. Intrauterine transmission occurred in greater than 50% during the 16 first weeks of pregnancy compared to 17% during the 21st to 24th weeks. Rubella defects appeared in a declining rate from 5/6 congenitally infected during the first 12 weeks to 1/7 at weeks 15 and 16. Three cases with deafness were found among the 65 children from earlier epidemics. Only 1 child with hearing impairment was found among children whose mothers were infected after the 16th week. Although rubella infections during the 17th to 24th weeks of pregnancy result in transmission to the fetus in about one fifth of cases, sequelae seem to be a rare event.

Evaluation of Assays for the Detection of Antibodies to Rubella. A Report Based on Data from the College of American Pathologists Surveys of 1982

L.P. Skendzel, K.R. Wilcox and D.C. Edson. Am J Clin Pathol 1983 Oct;80(4 Suppl):594-8.

Authors' abstract: Data from laboratories participating in the College of American Pathologists Surveys in 1982 provided information on the trends in testing for antibodies to rubella. Methods used by participants included: passive hemagglutination, 29%; latex agglutination card assay test, 25%; hemagglutination inhibition, 19%; enzyme immunosorbent assays, 13%; indirect fluorescent antibody assays, 11%; and radioimmunoassay, 3%. The results from these methods generally agreed well with the standard HI test, particularly for detection of immunity in negative and strongly positive samples. Laboratories should use caution, however, that the tests they use give satisfactory results with low titered sera. Compared to laboratories using the one to three-day-old chick cells with Heparin-MnCl2 for HI, laboratories using Human O Cells tended to get higher titers, and laboratories using Fixed Chick cell or Kaolin methods tended to get lower titers.

Fluorescence Immunoassay and Passive Latex Agglutination as Alternatives to Hemagglutination Inhibition for Determining Rubella Immune Status

S.L. Fayram, A. Nakasone, S. Aarnaes, M. Zartarian, E.M. Peterson and L.M. de la Maza. J Clin Microbiol 1983 Apr;17(4):685-8.

Authors' abstract: Three different assays for detection of rubella antibodies, hemagglutination inhibition (HAI), fluorescence immunoassay (FIA), and passive latex agglutination (PLA) were used to test 297 human serum samples. Overall agreements for immune status were as follows: HAI versus FIA, 95.3% (283 of 297); HAI versus PLA (1:10 dilution), 96.3% (286 of 297); HAI versus PLA (undiluted), 93.9% (279 of 297); PLA (1:10 dilution) versus FIA, 94.9% (282 of 297); and PLA (undiluted) versus FIA, 97.9% (291 of 297). The HAI test is the most time consuming, subjective, and technically difficult to perform. The FIA and PLA tests are very rapid and less labor intensive. In addition, the FIA offers an objective determination of the patient's rubella antibody level.

Use of Enzyme Immunoassays and the Latex Agglutination Test to Measure the Temporal Appearance of Immunoglobulin G and M Antibodies After Natural Infection or Immunization with Rubella Virus

J.M. Meegan, B.K. Evans and D.M. Horstmann. J Clin Microbiol 1983 Sep;18(3):745-8.

Authors' abstract: The time course of appearance of antibodies after infection with rubella virus was determined with an immunoglobulin G (IgG) detection enzyme-linked immunosorbent assay, a latex agglutination test, and an IgM detection enzyme-linked immunosorbent assay. In six naturally infected rubella patients and 26 vaccinees, antibodies measured by either the IgG enzyme-linked immunosorbent assay or the latex agglutination test generally appeared in parallel with those detected by the hemagglutination inhibition test. By 28 days after inoculation of live virus vaccine and by 2 days post-onset of clinical rubella symptoms caused by natural infection, antibodies were found by the two tests for all individuals. A commercially available enzyme-linked immunosorbent assay kit was used to detect rubella-specific IgM. After natural infection, IgM appeared earlier than IgG, and although IgM titers decreased rapidly postinfection, in four of five patients antibodies were still detectable 40 to 43 days after the onset of clinical symptoms. After vaccine-induced infection, rubella-specific IgM was lower in titer than after natural infection and was detected in only three of seven vaccinees 70 days post-immunization.

Rubella Antibodies Detected by Several Commercial Immunoassays in Hemagglutination Inhibition-Negative Sera

K.T. Kleeman, D.J. Kiefer and S.P. Halbert. J Clin Microbiol 1983 Nov;18(5):1131-7.

Authors' abstract: Although a very good correlation was found between the level of rubella antibodies measured by a standard hemagglutination inhibition (HI) test and by an enzyme-linked immunosorbent assay (ELISA) procedure (Cordia R), an appreciable proportion (31%) of ELISA-positive specimens were encountered among HI-negative sera. The reverse was rarely seen. Many of the HI-negative, ELISA-positive sera were also found to be positive for rubella antibodies by one or more other assay methods, including an immunofluorescence assay (IFA) procedure (FIAX), passive hemagglutination (PHA) (Rubacell and PHAST), latex agglutination (Rubascan), and a second ELISA procedure (Rubelisa). The specificity of all of the ELISA-positive HI-negative specimens was substantiated by absorption experiments. In these tests, the ELISA reactivities were blocked by rubella antigens, but not by a variety of tissue culture control antigens or by influenza virus grown on the same cell line. The findings indicate that many of the newer meth-

ods available for rubella antibody detection are more sensitive than HI for detecting low levels of rubella antibodies. Until more clinical information is available concerning the protective nature of these low levels of antibody, caution should be exercised in assessing the significance of these results.

Susceptibility to Rubella and Borderline Immunity

A. Fogel, B. Barnea and C.B. Gerichter. Isr J Med Sci 1983 Oct;19(10):934-5.

Authors' abstract: Immunity to rubella in women of childbearing age has been determined by hemagglutination inhibition (HI) and/or hemolysis in gel (HIG) methods. Susceptibility was defined as absence of antibody at a dilution of 1:16 in HI and a hemolysis zone of less than 7 mm in HIG tests. In screening 30,330 women during the years 1980-1981, 13.7% were found seronegative. Among 439 women immunized with RA-27/3 vaccine, 92% showed seroconversion, when tested by HI $\geq$2 months following vaccination. Paired sera from 35 vaccinees who remained seronegative were tested by two additional methods: sensitizing antibody (SA) and enzyme-linked immunosorbent assay (ELISA). Ten women were confirmed as vaccine failures by these two methods. The remaining women presented the following results: 19 had borderline and stable titers in their paired sera and 6 showed seroconversion, by SA and ELISA. These results indicate that both SA and ELISA are more sensitive than the HI and HIG tests for evaluation of rubella immunity and response to vaccination.

Epidemiology

Rubella Susceptibility in an Adolescent Female Population

K.A. Miller and T.D. Zager. Mayo Clin Proc 1984 Jan;59(1):31-4.

Authors' abstract: A survey of 1,008 adolescent girls was performed to characterize adolescent rubella immunity, and susceptibility was defined as a hemagglutination antibody titer of less than 1:8 (the definition used by the Minnesota State Health Department and the pediatric literature). The incidence of rubella susceptibility was 9.1% in the study population and was evenly distributed with regard to current age, age at time of vaccination, and source of vaccination. In subjects with a history of rubella vaccination, 7.4% were susceptible, whereas in the unvaccinated population, the susceptibility rate was 31.7%. Because rubella is a relatively benign disease except when acquired by the fetus during pregnancy, and adolescents are not only approaching the traditional age of motherhood but also experiencing pregnancy in increasing numbers, it is important for physicians to substantiate the rubella susceptibility status of their adolescent female patients.

Comparative Seroepidemiologic Observations of Rubella Infection in Pregnant Women and Female University Students

M.O. Paul and B.D. Paul. J Hyg Epidemiol Microbiol Immunol 1983;27(2):179-83.

Authors' abstract: Sera from 58 pregnant women and 34 female university students were tested by a hemagglutination-inhibition (HI) method to determine the levels of immunity to rubella and to assess factors important in its epidemiology. Ages of women ranged from 15 to 35 years. Pregnant women were from the lower socioeconomic groups, while students came from middle and upper income families. In both groups immunity to rubella increased with age. Students were more susceptible to the infection than pregnant women (21% compared with 3%, respectively)—$p<0.05$ and the geometric mean titer was significantly higher in pregnant women than in students. Since women were of the same ages and essentially from the same geographical location, it is suggested that differences in susceptibility rates to rubella were due to differences in the socioeconomic status of the two groups.

Seroepidemiologic Studies on Rubella in Fukuoka in Southern Japan During 1965-1981: Rubella Epidemic Pattern, Endemicity and Immunity Gap

K. Ueda, S. Nonaka, H. Yoshikawa, F. Sasaki, K. Segawa, H. Fujii, H. Tasaki, H. Shin, K. Tokugawa and T. Sato. Int J Epidemiol 1983 Dec;12(4):450-4.

Authors' abstract: The epidemiology of rubella in most areas of Asia has not been defined. In Fukuoka city in southern Japan, rubella epidemics occurred in 1956-1958, in 1966 and in 1976-1977. During the first halves of the 1960s and 1970s, neither epidemic nor endemic clinical rubella occurred. Rubella mass vaccination for girls of 14 years of age started in 1978. Rubella seroepidemiologic studies were performed in 1965, 1974, 1978-1979 and 1981 in Fukuoka city. Current studies indicated that children of 6-10 years of age during the epidemics of 1956-1958, 1966 and 1976-1977 were infected with rubella in 72%, 37% and 57% of cases, respectively. Just before the epidemics of 1966 and 1976-1977, 100% of the children under nine years of age had no antibodies to rubella, indicating absence of recent outbreaks. Whereas 95% of the population (young women of 15-18 years of age in 1981) who participated in the rubella mass vaccination program since 1978 have rubella HI antibodies, 46% of the nonparticipating population (19-23 years of age in 1981) remained susceptible to rubella. These facts indicate that rubella epidemics occurred in 1956-1958, 1966 and 1976-1977, that the magnitude of each epidemic was different, and that there were intervals without endemicity in the inter-epidemic periods. How-

ever, after the nation wide rubella epidemic in 1975-1977, endemic rubella continued, and rubella epidemics again occurred in 1980-1982. The unique rubella epidemic pattern in Japan may be changing in the 1980s to that which existed in most areas of the world where rubella was endemic with periodic increased incidence of epidemicity. Japanese rubella vaccination policy, which has left a definite immunity gap among young women in Fukuoka, should take into account the changing epidemic pattern of rubella.

Rubella and Congenital Rubella—United States, 1980-1983

Anonymous. MMWR 1983 Oct 7;32(39):505-10.

Authors' abstract: Although the incidence of reported rubella has fluctuated slightly over the past several years, a downward trend has been observed for most of the United States. A review of data for the period January 1, 1980, through September 24, 1983, indicates that if no sudden change in reporting patterns occurs, the final rubella incidence rate for 1983 should be at an all-time low.

In 1980, a total of 3,904 cases of rubella were reported to CDC; this represents an incidence of 1.7 cases per 100,000 population. The 1981 incidence (0.9/100,000) was the lowest reported since rubella became a notifiable disease in 1966; 2,077 cases were reported in 1981, a decline of 4.7% from the 1980 total. In 1982, 2,325 cases of rubella were reported in the United States (incidence 1.0/100,000)—a 12% increase over the 1981 total. The increased occurrence in 1982 reflected an increase in cases of rubella in California, primarily among adolescent and young-adult populations and particularly in hospitals and universities.

Incidence rates of confirmed and compatible congenital rubella syndrome (CRS) have declined substantially since 1979. Fifty-five cases were reported in 1979, 14 were reported in 1980, and nine were reported in both 1981 and 1982. California reported seven of the nine cases in 1982 and is the only state that has reported cases in 1983 (three cases, all with estimated dates of conception in 1982). Almost all CRS cases continue to be reported within the first year of birth.

Prevention and Control

Economic Evaluation of Different Vaccination Programs to Prevent Congenital Rubella

B. Stray-Pedersen. NIPH Ann 1982 Dec;5(2):69-83.

Author's abstract: Vaccination against rubella was introduced in Norway in 1978. Without any vaccination policy the frequency of congenital rubella is estimated at 0.4 per 1000 births. In this paper the consequences and effectiveness of the various vaccination programs are evaluated by applying a cost benefit model. Economically, all strategies to prevent congenital rubella turn out to be cost effective. However, based on the benefit/cost ratios and the net benefit the following recommendation can be made: vaccination, preferentially with the polyvalent vaccine, should be offered to all girls in puberty as a permanent running program. In addition, this policy should be supplemented for one or two decades with a program offering vaccination to non-immunized women after delivery and to women especially at risk of exposure. However, if the participation and acceptance rate of the vaccination is less than 100%, permanent vaccination offered at two different ages (i.e., in childhood and in puberty) gives the best results in the prevention of congenital cases.

Computer Assessment of Alternative Rubella Vaccination Strategies in New Zealand

R.C. Riseley, A.H. Smith, M. Laugesen and C.J. Chapman. NZ Med J 1983 Apr 13;96(729):235-8.

Authors' abstract: Results from a dynamic computer model of rubella vaccination programs indicate that consideration should be given to vaccinating all one-year-old girls and boys and revaccinating all girls at about 11 years of age, as well as continuing with the program for susceptible women in the childbearing age group. With vaccine-induced immunity decaying at about 1% annually, the vaccination of 80 to 95% of all one-year-olds, 95% of 11-year-old girls, and 5% of women aged 15 to 33 annually is expected to reduce congenital rubella syndrome deformities to less than 5% of the 1980 incidence by 1994, and to negligible levels thereafter. In comparison, continuation of the present scheme may reduce deformities to only 69% of 1980 levels by 1994 with a slow decline to 25% in 2010. (The 1980 levels used were computer generated to eliminate short-term fluctuations, and do not apply to actual figures from that year.) For convenience and better compliance, measles vaccine and the initial rubella vaccine may be given in combined form at 15 months without altering the effect of either. The rate of decay of immunity after vaccination is critically important in congenital rubella syndrome prediction, so that further accurate monitoring of immune status and congenital rubella incidence is essential.

Strategies for the Prevention of Congenital Rubella (French)

P. Buek...s. Rev Epidemiol Sante Publique 1983;31(3):283-8.

English summary: Screening for rubella in the beginning of pregnancy includes at least one assay for rubella antibodies. If a significant level of antibodies is found, two strategies are possible: 1) to consider the patient as protected if there is no other sign of rubella, or 2) to

assess the date of the infection in all cases, repeating the serological tests. In this paper we study the cost of this second strategy. Using a theoretical model of the rubella infection we calculated that the incidence of congenital rubella would be 9 cases in 10,000 newborns in populations with 10% of susceptible women at the age of 25. We studied the cost-effectiveness of a screening strategy including a second assay for rubella antibodies (inhibition of hemagglutination) after a positive one. This strategy is 10% more sensitive than a single test. Nevertheless, the cost of one case of congenital rubella prevented by this strategy is 13.3 higher than the cost of a case prevented by a strategy including the vaccination of boys and girls at the age of 2 years and of girls at the age of 12. Thus, the vaccination strategy is a priority for rubella prevention while the multiplication of the screening test is not a priority.

Current and Prospective Strategies for Controlling Congenital Rubella in the Czech Socialist Republic

J. Strauss. Zentralbl Gynakol 1983;105(16):1076-9.

According to a 1972 decree of the Ministry of Health, any pregnant woman who informs her gynecologist of exposure to rubella or who exhibits an exanthem suspected of being rubella must be tested serologically. The decree of the Ministry of Health concerning mass rubella vaccination of 12-year-old girls or female 6th-grade students is being implemented beginning with the 1982-1983 school year, with the administration of the attenuated rubella vaccine Almevax (RA-27 strain). With an almost 100% vaccination rate, as is usually the case for other vaccinations in the Czech Socialist Republic, by providing for the prolonged circulation of a relatively innocuous rubella virus, this strategy guarantees the "booster phenomenon" in the presence of a residuum of low humoral antibodies.

The dilemma concerning vaccination strategy in the CSR, however, has only partially been resolved at present since yearly vaccination of 12-year-old female schoolchildren would do nothing for women of childbearing-age years and beyond. For this reason, the targeted vaccination of women employed in health and education and puerperants, perhaps in pregnancy counseling offices, is being considered. A mass screening project in one of the ten regions of the CSR will help determine if targeted immunization should be conducted in the CSR.

Initial Results of Selective Rubella Vaccination in Czechoslovakia

V. Schwanzer, K. Borska, I. Masar and I. Schwanzerova. Zentralbl Gynakol 1983;105(16):1080.

From authors discussion: With the goal of preventing congenital rubella, since 1982 a complex program based on active immunization of rubella-susceptible girls and women has been conducted in the Czechoslovak Socialist Republic. The most important features of this program are:

1. Determination of immunity to rubella in 12- and 13-year-old girls (about 40,000 a year) and compulsory immunization of susceptible girls.
2. Testing of the immune status of all pregnant women as part of their prenatal care (approximately 120,000 a year) and recommendation of susceptible women postpartum.
3. Testing of all young women whose occupations expose them to a high risk of rubella infections (nurses, child care workers, teachers) and vaccination of susceptible women.
4. Testing of the staff of obstetrics and gynecology clinics, selection of susceptible persons (potential sources of infection for pregnant women) and vaccination of such persons.

Experience to date confirms the validity and feasibility of the proposed programs of rubella immunization in the Slovakian Socialist Republic.

Measles and Rubella on College Campuses: The Need to Act

K.J. Bart and D.H. Stenhouse. J Am Coll Health 1983 Oct;32(2):58-62.

Authors' abstract: The lack of immunization requirements at the nation's colleges and universities threatens the maintenance of the interruption of indigenous measles in the United States. The high susceptibility rates in some college populations coupled with the high mobility of college students who may travel to countries where measles is endemic or epidemic increases the potential for measles outbreaks.

Preventing measles in college-age populations is particularly important because the disease can be more serious in adults. In view of the importance of preventing measles in college students, the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service has recommended that officials strongly consider immunization requirements for college entry.

The ultimate goal of rubella immunization is the protection of a future fetus against damage from intrauterine infection. Although rubella cases are reported routinely on college campuses, most colleges make no effort at controlling these outbreaks or instituting immunization requirements. The ACIP strongly urges educational institutions to require proof of immunity to rubella for registration or employment.

Rubella Immunization History as a Guide to Immunity

C.E. Paul and E.S. Poole. J Epidemiol Community Health 1983 Mar;37(1):75-7.

Authors' abstract: If rubella immunization is highly effective, accurate recall of past immunization should

enable determination of immune state. The accuracy of recall was studied in a group of young adults aged 16-24 who had been offered Cendehill vaccination at school 10-11 years previously. The subjects were asked whether they had been vaccinated and blood was taken for rubella serology. School records of rubella immunization were compared with the histories of immunization. A positive history of immunization at school was correct in 32 out of 33 cases (97%). In contrast a negative history was accurate in only 14 out of 43 cases (33%). Ways of improving the memory of immunization are needed if this is to be used to determine immune state in young women.

Why Do Some Women Refuse Rubella Screening?

A. Hutchinson. J R Coll Gen Pract 1983 Apr;33(249):234-7.

From author's conclusion: The reasons why 250 women declined rubella antibody screening were elicited by a postal questionnaire.

From the compilation of the responses of the women who answered the questionnaire and the meager data available on those who made no contact, it appears that there are three broad groups from which can be made some predictions for future screening strategy:

1. The first group is comprised of those who have no need for screening—that is, those who wish to have no more children, have previously been found to be immune or have documentary evidence of vaccination.

2. In the second group are women who may have declined screening because of various commitments or problems which prevented them from accepting. These women could be reached by opportunistic screening, especially during consultations for family planning.

3. Finally there are those who are unlikely to accept screening except perhaps as part of antenatal care, or who prove impossible to contact. This group provides the best possible reminder of the value of the immunization program for schoolgirls.

By offering screening to all women of childbearing age in the practice, and identifying those who decline so that they may be offered opportunistic screening, the task of preventing intranatal rubella infection can be reduced to routine screening offered at one or two yearly intervals to girls aged 15-17 years. This is an easily managed task since the numbers are relatively small and, together with the school immunization program., should ensure that most young women are protected against rubella before childbearing begins.

Serology Testing as a Means of Encouraging Rubella Immunization

M.A. Brieseman and A.D. Milner. NZ Med J 1983 Oct 12;96(741):760-2.

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We take issue with all of those points. The best means of preventing rubella transmission in hospitals is through requiring that employees (both males and females) who might contract rubella from infected patients or if infected might transmit rubella to pregnant patients are immune.

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Authors' abstract: Rubella vaccination of children in the United States has resulted in a shift in the age of affected and susceptible individuals toward older age groups. In an effort to reduce the incidence of congenital rubella syndrome, the American Academy of Pediatrics and the Advisory Committee on Immunization Practices have recommended rubella vaccine for all male and female medical personnel who might contract and spread rubella to pregnant women. A survey of hospitals and outpatient practices in Little Rock, Arkansas, revealed extremely low compliance with the recommendation, suggesting the need for further education or legislation on rubella immunization for health care personnel.

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M.H. Hambling. J Infect 1980 Dec;2(4):341-6.

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Vaccination of Seronegative High-Risk Populations with Attenuated Rubella Vaccine

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Post-Partum Rubella Immunization: A Controlled Trial of Two Vaccines

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Authors' abstract: The effectiveness of two rubella vaccines (RA 27/3 and Cendehill) in women vaccinated post partum was compared. Significantly more women who received RA 27/3 gave satisfactory seroconversion responses than women who received Cendehill (97.6% *vs.* 82.2%). This difference was reflected in the geometric mean titers (43.6 *vs.* 17.0). More women who received RA 27/3 had minor side-effects, but the difference was not significant. The serological response to both vaccines was not affected by the concurrent administration of anti-D immunoglobulin. In view of these findings, the replacement of Cendehill vaccine with RA 27/3 vaccine for women vaccinated post partum should be considered.

assess the date of the infection in all cases, repeating the serological tests. In this paper we study the cost of this second strategy. Using a theoretical model of the rubella infection we calculated that the incidence of congenital rubella would be 9 cases in 10,000 newborns in populations with 10% of susceptible women at the age of 25. We studied the cost-effectiveness of a screening strategy including a second assay for rubella antibodies (inhibition of hemagglutination) after a positive one. This strategy is 10% more sensitive than a single test. Nevertheless, the cost of one case of congenital rubella prevented by this strategy is 13.3 higher than the cost of a case prevented by a strategy including the vaccination of boys and girls at the age of 2 years and of girls at the age of 12. Thus, the vaccination strategy is a priority for rubella prevention while the multiplication of the screening test is not a priority.

Current and Prospective Strategies for Controlling Congenital Rubella in the Czech Socialist Republic

J. Strauss. Zentralbl Gynakol 1983;105(16):1076-9.

According to a 1972 decree of the Ministry of Health, any pregnant woman who informs her gynecologist of exposure to rubella or who exhibits an exanthem suspected of being rubella must be tested serologically. The decree of the Ministry of Health concerning mass rubella vaccination of 12-year-old girls or female 6th-grade students is being implemented beginning with the 1982-1983 school year, with the administration of the attenuated rubella vaccine Almevax (RA-27 strain). With an almost 100% vaccination rate, as is usually the case for other vaccinations in the Czech Socialist Republic, by providing for the prolonged circulation of a relatively innocuous rubella virus, this strategy guarantees the "booster phenomenon" in the presence of a residuum of low humoral antibodies.

The dilemma concerning vaccination strategy in the CSR, however, has only partially been resolved at present since yearly vaccination of 12-year-old female schoolchildren would do nothing for women of childbearing-age years and beyond. For this reason, the targeted vaccination of women employed in health and education and puerperants, perhaps in pregnancy counseling offices, is being considered. A mass screening project in one of the ten regions of the CSR will help determine if targeted immunization should be conducted in the CSR.

Initial Results of Selective Rubella Vaccination in Czechoslovakia

V. Schwanzer, K. Borska, I. Masar and I. Schwanzerova. Zentralbl Gynakol 1983;105(16):1080.

From authors discussion: With the goal of preventing congenital rubella, since 1982 a complex program based on active immunization of rubella-susceptible girls and women has been conducted in the Czechoslovak Socialist Republic. The most important features of this program are:

1. Determination of immunity to rubella in 12- and 13-year-old girls (about 40,000 a year) and compulsory immunization of susceptible girls.

2. Testing of the immune status of all pregnant women as part of their prenatal care (approximately 120,000 a year) and recommendation of susceptible women postpartum.

3. Testing of all young women whose occupations expose them to a high risk of rubella infections (nurses, child care workers, teachers) and vaccination of susceptible women.

4. Testing of the staff of obstetrics and gynecology clinics, selection of susceptible persons (potential sources of infection for pregnant women) and vaccination of such persons.

Experience to date confirms the validity and feasibility of the proposed programs of rubella immunization in the Slovakian Socialist Republic.

Measles and Rubella on College Campuses: The Need to Act

K.J. Bart and D.H. Stenhouse. J Am Coll Health 1983 Oct;32(2):58-62.

Authors' abstract: The lack of immunization requirements at the nation's colleges and universities threatens the maintenance of the interruption of indigenous measles in the United States. The high susceptibility rates in some college populations coupled with the high mobility of college students who may travel to countries where measles is endemic or epidemic increases the potential for measles outbreaks.

Preventing measles in college-age populations is particularly important because the disease can be more serious in adults. In view of the importance of preventing measles in college students, the Immunization Practices Advisory Committee (ACIP) of the U.S. Public Health Service has recommended that officials strongly consider immunization requirements for college entry.

The ultimate goal of rubella immunization is the protection of a future fetus against damage from intrauterine infection. Although rubella cases are reported routinely on college campuses, most colleges make no effort at controlling these outbreaks or instituting immunization requirements. The ACIP strongly urges educational institutions to require proof of immunity to rubella for registration or employment.

Rubella Immunization History as a Guide to Immunity

C.E. Paul and E.S. Poole. J Epidemiol Community Health 1983 Mar;37(1):75-7.

Authors' abstract: If rubella immunization is highly effective, accurate recall of past immunization should

enable determination of immune state. The accuracy of recall was studied in a group of young adults aged 16-24 who had been offered Cendehill vaccination at school 10-11 years previously. The subjects were asked whether they had been vaccinated and blood was taken for rubella serology. School records of rubella immunization were compared with the histories of immunization. A positive history of immunization at school was correct in 32 out of 33 cases (97%). In contrast a negative history was accurate in only 14 out of 43 cases (33%). Ways of improving the memory of immunization are needed if this is to be used to determine immune state in young women.

Why Do Some Women Refuse Rubella Screening?

A. Hutchinson. J R Coll Gen Pract 1983 Apr;33(249): 234-7.

From author's conclusion: The reasons why 250 women declined rubella antibody screening were elicited by a postal questionnaire.

From the compilation of the responses of the women who answered the questionnaire and the meager data available on those who made no contact, it appears that there are three broad groups from which can be made some predictions for future screening strategy:

1. The first group is comprised of those who have no need for screening—that is, those who wish to have no more children, have previously been found to be immune or have documentary evidence of vaccination.

2. In the second group are women who may have declined screening because of various commitments or problems which prevented them from accepting. These women could be reached by opportunistic screening, especially during consultations for family planning.

3. Finally there are those who are unlikely to accept screening except perhaps as part of antenatal care, or who prove impossible to contact. This group provides the best possible reminder of the value of the immunization program for schoolgirls.

By offering screening to all women of childbearing age in the practice, and identifying those who decline so that they may be offered opportunistic screening, the task of preventing intranatal rubella infection can be reduced to routine screening offered at one or two yearly intervals to girls aged 15-17 years. This is an easily managed task since the numbers are relatively small and, together with the school immunization program., should ensure that most young women are protected against rubella before childbearing begins.

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Clinical Efficacy of Rubella Vaccine

W.L. Greaves, W.A. Orenstein, A.R. Hinman and W.S. Nersesian. Pediatr Infect Dis 1983 Jul-Aug;2(4):284-6.

Authors' abstract: In the period October 10, 1980, to January 19, 1981, 83 cases of rash illness compatible with rubella were reported in Sanford, Maine. Twenty-two (27%) were confirmed serologically. Forty cases (48%) occurred in Sanford High School students; the overall attack rate was 3.2%. A case-control study was undertaken to determine the effectiveness of rubella vaccine in preventing clinical rubella. Bayes' theorem was used to calculate the attack rates in the vaccinated population (ARV) and the unvaccinated population (ARU). Vaccine efficacy (VE), calculated with use of the formula VE (%) = [(ARU − ARV)/ARU] x 100, was 90%. These results indicate that rubella vaccine is highly effective in preventing clinical rubella and do not support proposals for routine revaccination.

Serological Response to Rubella Revaccination in Adolescent Females

S.B. Fitzpatrick, R. Anthony and F. Heald. J Adolesc Health Care 1983 Sep;4(3):168-70.

Authors' abstract: The study's purpose was to utilize ELISA in determining rubella susceptibility in teenagers who are seronegative by HI. Ten previously vaccinated, seronegative adolescent females were revaccinated with RA 27/3 and their IgG and IgM responses measured by ELISA. Before revaccination, all 10 were seronegative for rubella by HI (<1:10). However, by ELISA, six showed an IgG and no IgM levels. After reimmunization, three showed a significant IgM response by day 6, indicating primary rubella exposure. The remaining seven females failed to demonstrate an IgM response; however, the failure was consistent with a history of prior rubella vaccination. Peak IgG responses were noted by day 12 in nine of the females. The remaining teenager failed to show an IgG response and was considered a vaccine failure. This study confirms the superiority of ELISA as compared to HI titers in determining rubella susceptibility.

Serological Response to Rubella Revaccination

M.K. Serdula, S.B. Halstead, N.H. Wiebenga and K.L. Herrmann. JAMA 1984 Apr 20;251(15):1974-7.

Authors' abstract: To document the serological response, 21 seronegative rubella vaccinees (hemagglutination inhibition [HI] titer less than 10) were revaccinated with RA 27/3 rubella vaccine. All demonstrated an anamnestic response. Although RA 27/3 vaccine was an effective booster, antibody boost was not maintained in some persons. Of 15 persons tested, 24 to 27 months after revaccination, six had a significant HI antibody drop (fourfold or greater); only one had lost all detectable HI antibody. Although all 21 study participants were initially HI seronegative by rubella HI testing, 16 (76.2%) possessed neutralization and/or enzyme-linked immunosorbent assay antibodies before revaccination. As more persons with vaccine-induced immunity join the adult population pool, more sensitive test methods may be needed to assess serological status accurately.

Rubella Vaccination During Pregnancy—United States, 1971-1982

Anonymous. MMWR 1983 Aug 26;32(33):429-32, 437.

Authors' abstract: From January 1971 to December 1982, 959 pregnant women who received rubella vaccine either within 3 months before or 3 months after their presumed dates of conception were reported to CDC. These women were followed prospectively to determine the risk of fetal abnormalities following exposure to the vaccine.

Twenty-eight (35%) of the 81 susceptible mothers were vaccinated with the RA 27/3 vaccine during the highest risk period for viremia and fetal defects (1 week before to 4 weeks after conception). Neither those infants nor any others were born with CRS; therefore, the observed risk of CRS following rubella vaccination continues to be zero. The theoretical maximum risk for the occurrence of CRS in this group of 83 children, however, based on the 95% confidence limits of the binomial distribution, may be as high as 5%. (If the 95 infants exposed to the other rubella vaccines are included, the maximum theoretical risk is 2%.) This overall maximum risk remains far less than the 20% or greater risk of CRS associated with maternal infection with wild rubella virus during the first trimester of pregnancy.

Following an earlier review of these data, the Immunization Practices Advisory Committee (ACIP) stated in 1981 that: (1) pregnancy remains a contraindication to rubella vaccination because of the theoretical, albeit small, risks of CRS; (2) reasonable precautions be taken to preclude vaccination of pregnant women, including asking women if they are pregnant, excluding those who say they are, and explaining the theoretical risks to others; and (3) if vaccination does occur within 3 months of conception, the risk of CRS is so small as to be negligible; thus, rubella vaccination of a pregnant woman should not in itself indicate interruption of pregnancy. The patient and her physician, however, should make the final decision. Data collected through 1982 continue to support these recommendations.

Reactions to Rubella Immunizations in Adult Clients of an Employee Health Setting

S. Gobin, D. Cardellino, B. Duryea, C. Rager and D. Shields. Occup Health Nurs 1983 Apr;31(4):15-9, 47.

Authors' abstract: This study, conducted in a large city hospital in western Pennsylvania, researched the hypotheses: 1. Synovial symptoms develop less often than rash

reactions in adults who receive the rubella vaccine; and 2. synovial symptoms are more uncomfortable than rash reactions in adults who receive the rubella vaccine. Subjects participating in this research study included 23 adult employees, ranging in age from 23-48 years who received rubella immunization. The subjects were proven rubella non-immune on two separate serum specimens, and reported some type of a reaction within 30 days after receiving the immunization.

The instrument used in this study was a nine-point questionnaire. Reaction experienced by the subjects to the rubella immunization included: rash, synovial symptoms, lymph node enlargement, fever and one case of pneumonia. Within the study it was found that the majority of the sample—78.3% (18 employees)—developed a rash, and only 56.7% (13 employees) of the sample experienced synovial symptoms. A discomfort level scale of none, mild, moderate, and severe was used. Of the employees experiencing joint reactions, 69.2% (nine employees) found the discomfort level moderate or severe. Of the employees experiencing rash reactions, only 33.3% (six employees) found the discomfort level moderate and none felt the rash was severe.

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INFLUENZA

General

Construction and Characterization of an Infectious Vaccinia Virus Recombinant That Expresses the Influenza Hemagglutinin Gene and Induces Resistance to Influenza Virus Infection in Hamsters

G.L. Smith, B.R. Murphy and B. Moss. Proc Natl Acad Sci USA 1983 Dec;80(23):7155-9.

Authors' abstract: A DNA copy of the influenza virus hemagglutinin gene, derived from influenza virus A/Jap/305/57 (H2N2) was inserted into the genome of vaccinia virus under the control of an early vaccinia virus promoter. Tissue culture cells infected with the purified recombinant virus synthesized influenza hemagglutinin, which was glycosylated and transported to the cell surface where it could be cleaved with trypsin into HA1 and HA2 subunits. Rabbits and hamsters inoculated intradermally with recombinant virus produced circulating antibodies that inhibited hemagglutination by influenza virus. Furthermore, vaccinated hamsters achieved levels of antibody similar to those obtained upon primary infection with influenza virus and were protected against respiratory infection with the A/Jap/305/57 influenza virus.

Ribavirin Aerosol Treatment of Influenza B Virus Infection

W. McClung, V. Knight, E. Gilbert, Z. Wilson, M. Quarles and G.W. Divine. JAMA 1983 May 20;249(19): 2671-4.

Authors' abstract: In a randomized, controlled study, ribavirin small-particle aerosol was found to be effective in the treatment of influenza B virus infection in a group of college students. Eleven treated patients experienced significantly more rapid defervescence, disappearance of systemic illness, and reduction of virus shedding in nasal secretions than ten control patients treated with a saline aerosol. Antibody response to infection was similar in both groups. The treatment was well tolerated, and hematologic and clinical chemical tests demonstrated no toxicity. The estimated dose of ribavirin aerosol retained was about 2 g in 39 hours of treatment during the first 60 hours in the hospital.

Reduction in Fever and Symptoms in Young Adults with Influenza A/Brazil/78 H1N1 Infection After Treatment With Aspirin or Amantadine

W. Younkin, F. Betts, K. Roth and R.G. Douglas, Jr. Antimicrob Agents Chemother 1983 Apr;23(4):577-82.

Authors' abstract: During an outbreak of influenza A/Brazil/78 H1N1 infection, 47 volunteers with clinical and virological influenza of less than 2 days duration were treated in a randomized double-blind fashion for 5 days with 100 or 200 mg of amantadine daily or with 3.25 g of aspirin daily. The aspirin treatment group defervesced more rapidly (10.3 hours versus 21.5 hours and 23.6 hours, $p<0.01$), but by the second daily follow-up visit, both groups of amantadine recipients exhibited greater symptomatic improvement. Bothersome side effects resulted in discontinuation of therapy by 35% of the aspirin treatment group but only 3% of the amantadine treatment group ($p<0.05$). Individuals who present to a physician during an influenza A epidemic with characteristic symptoms will experience symptomatic benefit from amantadine treatment, with negligible toxicity.

Clinical and Laboratory

Immunity to Influenza in Man

R.B. Couch and J.A. Kasel. Annu Rev Microbiol 1983; 37:529-49.

Authors' abstract: The observations summarized in this review indicate immunity to infection with type A influenza viruses is subtype specific since little or none is conveyed to subtypes possessing immunologically distinct HA and NA proteins. However, within a subtype, a prior antigenic experience with one variant may prevent or modify illness to another. The resulting degree of subtype

immunity depends on the extent of relatedness between variants. Observations with H3N2 viruses indicate that homotypic resistance to subsequent infection and illness with the same virus is potent and of relatively long duration. The long lasting durability of such immunity was indicated by the epidemiologic pattern following the reappearance of H1N1 virus. Knowledge of the duration and specificity of immunity aids considerably in assessing mechanisms that account for host resistance to influenza. Recovery from influenza virus infection must involve a variety of humoral and cell-mediated immune mechanisms, and conclusions regarding the relative importance of each one are not possible at present. To prevent infection, involved immune mechanism(s) must account for: (a) subtype specificity, (b) reduced cross-reactivity of immunity for succeeding antigenic variants, (c) a long duration of immunity, and (d) immunity at the mucosal surface. Only antibody directed toward the HA molecule presently satisfies these properties and thus should be considered the major mediator of resistance to infection. Study of naturally occurring infection is needed for determining the duration and specificity of secretory IgA in nasal and lower respiratory secretions so as to establish its relative importance as a mediator of immunity. However, the described duration, specificity, and consistent relationship to immunity suggest that IgG antibody in respiratory secretions, derived entirely or partly from serum, is the most likely mediator of resistance to natural influenza.

The Importance of Antineuraminidase Antibodies in Resistance to Influenza A and Immunologic Memory for Their Synthesis

A.N. Naikhin, I.M. Tsaritsina, E.V. Oleinikova, L.G. Syrodoeva, N.L. Korchanova, G.M. Denisov and YaS. Shvartsman. J Hyg (Lond) 1983 Aug;91(1):131-8.

Authors' abstract: Eight hundred and seventy-seven sera from 360 adults aged 18-50 who were under permanent observation from October 1980 to March 1981 have been studied by hemagglutination-inhibition (HI) and erythrocyte elution-inhibition (EI) tests—a simplified method of antineuraminidase antibody titration. It was demonstrated in some subjects infected with influenza A H1N1 and H3N2 viruses that the antibody rise was to one of the surface antigens only—hemagglutinin or neuraminidase. These subjects made up 5.2-25.8% of all examinees. The protective effect of antibodies to neuraminidase was similar to that of antihemagglutinins. Interaction of both types of antibodies was observed in protection against the disease. Data have been obtained on the influence of antineuraminidase antibodies in decreasing the severity of natural infection with influenza A. A study of heterologous immunologic responses to hemagglutinin and neuraminidase among persons immunized with live influenza A H1N1 and H3N2 vaccines and among children naturally infected with influenza A H3N2 demonstrated the presence of immunologic memory for antineuraminidase antibody synthesis. Thus, the suggestion of a common antigenic structure for neuraminidase N1 and N2 is made.

Direct Isolation of H1N2 Recombinant Virus from a Throat Swab of a Patient Simultaneously Infected with H1N1 and H3N2 Influenza A Viruses

F. Nishikawa and T. Sugiyama. J Clin Microbiol 1983 Aug;18(2):425-7.

Authors' abstract: Two H1N2 recombinant viruses were isolated by a plaquing method from a throat swab of a patient who was simultaneously infected with H1N1 and H3N2 influenza viruses during the Tokyo epidemic of 1981. This is the first direct evidence that recombination of influenza viruses occurred in the human body.

Epidemiology

Variation in Frequency of Natural Reinfection with Influenza A Viruses

A.L. Frank and L.H. Taber. J Med Virol 1983;12(1):17-23.

Authors' abstract: To investigate the frequency of natural reinfection with influenza A viruses, 55 children followed from birth along with the 44 other children and 85 adults in their families were observed for varying periods between 1975 and 1981 in the Houston Family Study. Persons infected in 1976 or early 1977 with influenza A subtype H3N2 experienced a high rate of reinfection during the 1977-1978 season (63% in one group of young children) and additional reinfections in 1980-1981. Persons in whom H3N2 infection was first observed in 1977-1978 had little or no reinfection in 1980-1981, one reinfection was observed in 1980-1981 among 19 young children at risk. Only one reinfection with influenza A subtype H1N1 was observed following introduction of the virus in early 1978 despite exposure in 1978-1980 and a substantial outbreak in 1980-1981. Statistically significant protection from reinfection in young children followed from birth was not noted for the 1977-1978 H3N2 outbreak but was present in 1979-1981 for both H3N2 and H1N1 viruses. Reasons for variations in reinfection suggested by this data include 1) socioeconomic and other factors influencing intensity of exposure, 2) age at primary infection, 3) varying degrees of antigenic difference between sequential variants of a major subtype, and 4) unrecognized immunogenicity or virulence differences between subtypes and variants.

Procedures for Estimating Transmission Parameters from Influenza Epidemics: Use of Serological Data (Russian)

I.M. Longini, Jr., J.S. Koopman and A.S. Monto. Vopr Virusol 1983 Mar-Apr;(2):176-82.

Authors' abstract: A maximum likelihood procedure is given for estimating household and community transmission parameters from observed influenza infection data. The mathematical model used does not require the specification of infection onset times and, therefore, can be used with serological data which detect asymptomatic infections. Infection data was derived by serology and virus isolation from the Tecumseh Respiratory Illness Study and the Seattle Flu Study for the years 1975-1979. Influenza A (H1N1), A (H3N2), and B viruses were found to be in descending order both in terms of ease of spread in the household and intensity of the epidemic in the community except when two strains co-circulate. Children are found to be the main introducers of influenza into households.

Effect of Influenza Epidemics on Acute Respiratory Morbidity of Noninfluenzal Etiology (Russian)

L.Iu. Taros and A.A. Smorodintsev. Zh Mikrobiol Epidemiol Immunobiol 1983 May;(5):64-7.

English summary: The use of correlation analysis has made it possible to reveal a high degree of influence exerted by influenza epidemics on morbidity rate in adenoviral, respiratory-syncytial, parainfluenza and mycoplasmic infections among the population. During the months of influenza epidemic considerable concomitant incidence of respiratory-syncytial, adenoviral and especially mixed infections was observed in all age groups in comparison with periods free from influenza epidemic. The study of concomitant morbidity during the periods of 6 influenza A (H3N2) epidemics and 3 influenza B epidemics has shown that the immunosuppressive activity of influenza virus, leading to the activation of other causative agents of acute respiratory diseases, reaches its highest level at the periods of influenza A epidemics characterized by a more intensive and severe clinical course of the disease, such as in influenza A/Victoria/35/72 (H3N2), and drops to a minimum at the periods of influenza B epidemics.

Epidemiological Analysis of the Influenza Virus A Carrier State in Healthy Children (Russian)

L.S. Karpova, T.L. Popova, N.A. Ivanova, E.A. Zibina and V.L. Ivanova. Vopr Virusol 1983 May-Jun;(3):286-9.

English summary: Clinical and laboratory examinations in two permanently observed children's institutions were carried out in 1968-1978. Altogether, 241 children were examined virologically 759 times, of them 181 children were found to be truly healthy. In the epidemic period the latter yielded virus in 3.7%, in the interepidemic period in 1%. Unlike asymptomatic infection, transitory virus carrier state was not accompanied by antibody production, and in a number of such cases subsequently led to an overt clinical disease.

An Outbreak of Type C Influenza in a Children's Home

S. Katagiri, A. Ohizumi and M. Homma. J Infect Dis 1983 Jul;148(1):51-6.

Authors' abstract: During a one-year survey of a children's residence housing 20 young children and employing 29 adults, a confirmed outbreak of type C influenza unassociated with other known respiratory infections was studied. Seventeen of 20 children and two of the nine employees studied developed symptoms, which were characterized primarily by fever and nasal discharge. The three children who did not contract the disease were all under three months of age. Thirteen strains of virus were recovered from throat-swab specimens: 12 from children and one from an adult. All isolates were identified serologically as type C influenza virus. Evidence of reinfection was found in a two-year-old child and two adults who developed increases in antibody titers, the virus was recovered from a throat-swab specimen from one of these adults.

Surveillance of Influenza in Houston, Texas, USA: Gradual Transition from A/Victoria/75 (H3N2) to A/Texas/77 (H3N2) Predominance and Antigenic Characterization of "Intermediate" Strains

J.G. Velazco, R.B. Couch, H.R. Six and W.P. Glezen. Bull WHO 1983;61(2):345-52.

Authors' abstract: Influenza epidemics in Houston, Texas, USA, during the winter of 1975-1976, 1976-1977, and 1977-1978 were attributed to A/Victoria/3/75 (H3N2), B/Hong Kong/5/72, and A/Texas/1/77 (H3N2)-like viruses, respectively. Both A/Victoria and A/Texas viruses were detected towards the end of the 1976-1977 epidemic and throughout the 1977-1978 epidemic. To determine if there had been a gradual transition in the predominant strain, 267 viral isolates from the 1975-1976 epidemic were tested for A/Texas virus. Eight specimens (3%) that appeared to contain A/Texas antigens were cloned and retested with specific antisera prepared in guinea-pigs and ferrets. One virus was identical to A/Texas/1/77 virus, two reacted like A/Victoria/3/75 and five reacted equally well with antisera prepared against A/Victoria/3/75 and A/Texas/1/77 viruses (bridging strains). The six viral isolates containing A/Texas antigens were obtained at different times during the epidemic, from all parts of the city from males and females aged between 1 and 20 years.

Characterization of type A influenza virus isolates obtained during the 1976-1977 and 1977-1978 epidemics revealed a progressive increase in the frequency of viruses containing A/Texas antigens, from 2.2% in 1975-1976 to 32% in 1976-1977 to 70% in 1977-1978. Thus, both type A (H3N2) variants were present in the Houston community in 3 successive years.

An antigenic analysis of the bridging viruses was performed by competition radioimmunoprecipitation assays and by reactivity with a set of monclonal antibodies prepared against A/Texas/1/77 virus. These assays confirmed the identity of A/Texas isolate with the prototype virus and indicated that the bridging strains shared antigenic determinants with both A/Vic/75 and A/Tex/77 viruses, but were more closely related to A/Victoria/3/75 virus.

It seems clear that new variants of a subtype of type A influenza may not immediately displace the existing variant and that seeding in a community and transition from predominance of one variant to another may be a gradual process.

Influenza B Virus Infections in the Community and the Family. The Epidemics of 1976-1977 and 1979-1980 in Houston, Texas

A.L. Frank, L.H. Taber, W.P. Glezen, E.A. Geyer, S. McIlwain and A. Paredes. Am J Epidemiol 1983 Sep;118(3):313-25.

Authors' abstract: Influenza B virus epidemics occurred in Houston, Texas, in 1976-1977 and 1979-1980. Among families with young children followed longitudinally in the Houston Family Study, 112 infections were detected during 511 person-years of observation. The infection rates for the two epidemics were similar—24 per cent and 20 per cent—although the two epidemics differed greatly in the community. The first epidemic was much more intense with a mid-winter peak that produced school absentee rates above 12 per cent for four consecutive weeks. The indolent epidemic of 1979-1980 smoldered from late September to mid-April with a peak during the second week of March for which school absenteeism did not exceed 8 per cent. In the Houston Family Study population, the combined infection rate for the two outbreaks was highest at 35 per 100 person-years for school children aged 6-19 years. Preschool children aged 7 months-5 years and adults had infection rates of 31 and 16 per 100 person-years, respectively. Preexisting neutralizing antibody titers $\geq$3.5 log2 protected against influenza B infection and illness. Preschool children above 6 months of age, school age children, and parents introduced infection into the family at rates of 15, 15, and 9 per 100 person-years, respectively. Three second introductions were observed. The secondary infection rate was highest among school-aged children at 61 per 100 persons at risk.

Prevention and Control

Influenza Vaccination

M.A. Riddiough, J.E. Sisk and J.C. Bell. JAMA 1983 Jun 17;249(23):3189-95.

Authors' abstract: Cost-effectiveness analysis was used to evaluate influenza vaccination. From 1971-1972 through 1977-1978, vaccination of an elderly person 65 years of age or older saved net medical care costs while improving health. Vaccination of younger high-risk adults aged 15 through 64 years also improved health for a low net cost per year of healthy life gained. By covering influenza vaccination during those years, the Medicare program would have incurred a net cost for each vaccination of $13 per year of healthy life gained for medical costs connected with influenza and $791 per year gained including costs of treating other illnesses in later life. The analysis indicates the need for epidemiologic research on the extent of influenza and the mechanism of its spread. The results also raise the issue of public policy to promote influenza vaccination among high-risk persons as a low-cost, preventive technology.

Clinical Reactions and Antibody Responses to Influenza Vaccines. A Comparison of Split or Subunit Vaccines in Children and Young Adults

D.I. Bernstein and J.D. Cherry. Am J Dis Child 1983 Jul;137(7):622-6.

Authors' abstract: The reactogenicity and immunogenicity of a trivalent split-product influenza vaccine and a trivalent subunit influenza vaccine were studied in 67 children and young adults. Subjects received two doses of either vaccine given one month apart. The reactogenicity of the two vaccines was similar. After the second dose of the split-product vaccine, the prevalence of hemagglutination-inhibiting (HAI) antibody titers of 20 or more was as follows: A/Brazil/78, 73%, A/Bangkok/79, 100%, and B/Singapore/79, 73%. Similar data for the subunit vaccine recipients were 78%, 100%, and 74%, respectively. The HAI antibody responses to the A/Brazil/78 and B/Singapore/79 antigens of both vaccines were relatively poor in those subjects who were initially seronegative (HAI antibody titer less than 5) to the specific antigen.

Immune Responses in Serum and Respiratory Secretions Following Vaccination with a Live Cold-Recombinant (CR35) and Inactivated A/USSR/77 (H1N1) Influenza Virus Vaccine

J.M. Zahradnik, J.A. Kasel, R.R. Martin, H.R. Six and T.R. Cate. J Med Virol 1983;11(4):277-85.

Authors' abstract: One hundred adult volunteers were administered inactivated vaccine (20 micrograms/0.5 cc)

intramuscularly (IM) or intranasally (IN), or $10^{4.7}$ TCID50 of a live cold-adapted vaccine (CR35) IN. Microneutralization (Nt) and radioimmunoprecipitation methods were employed to measure hemagglutinin antibody responses in sera, nasal washes, and in bronchopulmonary lavage fluids. In unprimed recipients, the relative frequency of serum antibody response and magnitude of rise was highest following the IM-inactivated vaccine (100%) and lowest after IN-live vaccine (29%). However, in individuals with pre-existing antibody, the three vaccines given were comparably immunogenic. Occurrences of secretory IgA hemagglutinin antibody in nasal washings were more frequently associated with topical administration of live or inactivated vaccine, whereas, IgG hemagglutinin antibody responses occurred with equal frequency in nasal washings in all three vaccine groups. Analysis of the hemagglutinin antibody responses in the lower respiratory tract showed that the IN-live vaccine favored the induction of secretory IgA hemagglutinin antibody and the IM-inactivated vaccine stimulated a more frequent IgG hemagglutinin antibody response.

A Comparison of Live and Inactivated Influenza A (H1N1) Virus Vaccines. 2. Long-Term Immunity

A. Clark, C.W. Potter, R. Jennings, J.P. Nicholl, A.F. Langrick, G.C. Schild, J.M. Wood and D.A. Tyrrell. J Hyg (Lond) 1983 Jun;90(3):361-70.

Authors' abstract: Groups of volunteers were immunized with one of three influenza virus vaccines, and the resistance to challenge infection with attenuated influenza A (H1N1) virus was measured 8 months later. The vaccines were aqueous subunit influenza A/USSR/77 (H1N1) vaccine, aqueous subunit influenza B/Hong Kong/73 vaccine, or attenuated influenza virus A (H1N1) vaccine. The B virus vaccine was included as a control to assess the incidence of natural A virus infection during the study period. A proportion of the B virus vaccinees had pre-existing A (H1N1) virus antibody and were used to study the immunity conferred by natural infection to the live virus challenge. The serum antibody responses were measured at 1 and 8 months after immunization. The results showed that all the vaccines induced serum HI antibody in a proportion of the volunteers; however, after 1 month, higher titers of serum antibody were found in volunteers given inactivated A vaccine than in those given live attenuated A virus vaccine. Eight months post-immunization the titers of serum antibody in volunteers given inactivated vaccine had declined significantly, but there were no changes in the antibody titers of those given live virus vaccine. The incidence of infection by the challenge virus at 8 months post-immunization was directly related to the serum antibody titers 1 month post-immunization, no evidence was obtained to suggest that those given live virus vaccine had a more solid immunity than those given inactivated vaccine.

Summary of Clinical Trials of Inactivated Influenza Vaccine—1978

J.R. La Montagne, G.R. Noble, G.V. Quinnan, G.T. Curlin, W.C. Blackwelder, J.I. Smith, F.A. Ennis and F.M. Bozeman. Rev Infect Dis 1983 Jul-Aug;5(4): 723-36.

Authors' abstract: This report summarizes the clinical trials of the A/USSR/77 (H1N1) influenza vaccines performed in 1978. A total of 2,091 subjects participated in these trials. The results of these clinical trials indicated that two doses of H1N1 viral antigen were necessary to produce serum titers of hemagglutinin-inhibiting (HAI) antibody of greater than 1:40 in 80% or more of the test subjects younger than 25 years of age, who were unlikely to have experienced natural infection during the earlier period of prevalence of H1N1 virus (1947-1957). Only one dose of the A/Texas/77 (H3N2) or B/Hong Kong/72 antigen was necessary to stimulate equivalent titers of HAI antibody in serum. Thus, previous natural exposure to H1N1 viruses primed individuals 26 years of age or older to respond to H1N1 antigens. No major differences in antigenicity were noted between whole-virus and split-virus vaccines. No differences in reaction indexes measuring systemic reactions were noted when vaccine types were compared. Only one vaccine was associated with a reaction index appreciably higher than that of placebo. The relatively uniform antibody responses observed were attributed to the newer methods of vaccine standardization introduced after the clinical trials in 1976. No cases of vaccine-related neurological problems, including Guillain-Barré syndrome, were found during these trials. Vaccines containing 7-21 micrograms of each viral antigen were antigenic and were well tolerated.

Antigenicity and Reactogenicity of Influenza A/USSR/77 Virus Vaccine in Children—A Multicentered Evaluation of Dosage and Safety

P.F. Wright, J.D. Cherry, H.M. Foy, W.P. Glezen, C.B. Hall, K. McIntosh, A.S. Monto, R.H. Parrott, B. Portnoy and L.H. Taber. Rev Infect Dis 1983 Jul-Aug;5(4): 758-64.

Authors' abstract: Clinical trials of monovalent A/USSR/77 (H1N1) and trivalent A/USSR/77 (H1N1), A/Texas/77 (H3N2), and B/Hong Kong/72 inactivated influenza virus vaccines were carried out in 358 children and adolescents. Only split-virus vaccines were administered to children younger than 13 years of age. No serious local or systemic reactions were observed among the study participants. Two doses of vaccine containing 7-20 micrograms of the A/USSR/77 (H1N1) viral antigen were required to achieve serum titers of hemagglutinin-inhibiting (HAI) antibody greater than 1:40. However, single doses containing 7-20 micrograms of the A/Texas/77 (H3N2) or B/Hong Kong/72 antigens stimulated serum HAI antibody levels of 1:40.

Influenza and Pneumococcal Immunization in Medical Clinics, 1978-1980

E.R. Ratner and D.S. Fedson. Arch Intern Med 1983 Nov;143(11):2066-9.

Authors' abstract: In 1978 to 1979, the General Medicine Clinic (GMC) immunization program at the University of Chicago immunized 54% of 1,543 high-risk patients with influenza vaccine. In 1979 to 1980, 45% of 1,462 high-risk patients were immunized, including 72% of the patients who had been immunized the year before. Many patients who were immunized were initially undecided or did not want the vaccine. In 1978 to 1980, pneumococcal vaccine was given to 784 GMC patients, including 24% of 2,229 high-risk patients seen at least once during the two immunization program periods. Twenty-two patients (2.8%) were inadvertently reimmunized. The GMC programs were approximately seven to ten times more effective in immunizing patients than were physicians in medical subspecialty clinics without such programs. Since many patients hospitalized with influenza and pneumonia have recently received care in hospitals, organized programs for immunization in hospitals could make a substantial contribution to the prevention of these diseases.

Influenza A Prophylaxis With Amantadine in a Boarding School

D.K. Payler and P.A. Purdham. Lancet 1984 Mar 3;1(8375):502-4.

Authors' abstract: In a boarding school for boys, where routine influenza vaccination is carried out annually, 267 boys were given amantadine (100 mg daily) and 269 received no specific treatment during an influenza A (H1N1) outbreak. Three boys receiving amantadine and 29 boys receiving no medication had laboratory-proven influenza A. There are circumstances when the prophylactic use of amantadine may be justified for the control of influenza A outbreaks in boarding schools and other institutions where high attack-rates are experienced.

Estimation of the Probability that Guillain-Barré Syndrome Was Caused by the Swine Flu Vaccine: U.S. Experience (1976-1977)

R.L. Greenstreet. Med Sci Law 1984;24(1):61-7.

Author's summary: A statistical method was presented for determining the probability that cases of Guillain-Barré syndrome (GBS) among residents of the United States and Puerto Rico who participated in the 1976-77 swine flu vaccine program were due to the vaccine. It was determined that the vaccine (A/New Jersey) was the most likely cause of GBS if the onset was within five weeks after vaccination. From the sixth to the tenth week after vaccination, the association was unlikely. After the tenth week, the association between the vaccine and GBS was negative.

Effect of Influenza Vaccine on Warfarin Anticoagulation

P. Kramer, M. Tsuru, C.E. Cook, C.J. McClain and J.L. Holtzman. Clin Pharmacol Ther 1984 Mar;35(3):416-8.

Authors' abstract: Recent studies have indicated that viral infections, influenza vaccination, or drugs that increase interferon synthesis all decrease hepatic drug metabolism. We report a case in which influenza vaccination was temporally related to an increased anticoagulant effect of warfarin. A prospective study evaluating the effect of influenza vaccination on the prothrombin time of eight patients anticoagulated over the long term showed that there was prolongation of prothrombin time of 40%. In a second study, the effect of influenza vaccination on warfarin t1/2 was determined in healthy subjects. No significant effect on warfarin metabolism was observed after vaccination. We conclude that influenza vaccination is associated with increased anticoagulant response in some patients receiving anticoagulants over a long term. This effect appears to be related to some step in the coagulation pathway and not to decreased warfarin metabolism and a subsequent rise in serum concentration.

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DIPHTHERIA—PERTUSSIS—TETANUS

General

Immunologic Response to Early and Routine DTP Immunization in Infants

L.J. Baraff, R.D. Leake, D.G. Burstyn, T. Payne, C.L. Cody, C.R. Manclark and J.W. St. Geme, Jr. Pediatrics 1984 Jan;73(1):37-42.

Authors' abstract: The effect of early immunization, prior to discharge from the newborn nursery, on subsequent immunity as determined by enzyme-linked immunosorbent assay (ELISA) immunoglobulin (Ig) M and IgG antibody titers to filamentous hemagglutinin and lymphocytosis-promoting toxin (LPT) of *Bordetella pertussis* and by standard pertussis agglutinin titers was investigated. Eighteen infants received routine diphtheria-tetanus-pertussis (DTP) immunization at 2, 4, and 6 months of age; 17 other infants received routine immunization and an additional DTP immunization in the newborn nursery. Antibody was determined on samples of cord blood and whole blood obtained at 4, 6, and 9 months of age. IgM anti-filamentous hemagglutinin was significantly higher at 4 and 6 months of age in the group that received early immunization ($p < .05$). There was no significant difference in IgM anti-LPT, IgG anti-filamentous hemagglutinin, IgG anti-LPT, or pertussis agglutinin antibodies. Six control infants had high cord IgG anti-LPT titers. These six infants had significantly lower antibody titers to LPT at 6 and 9 months of age when compared with control infants with lower cord titers. Thirteen infants in the early immunization group with lower cord IgG anti-LPT titers achieved significantly lower titers at 9 months of age than the 12 comparable infants in the control group.

A 7-Year Survey of Disorders Attributed to Vaccination in North West Thames Region

T.M. Pollock and J. Morris. Lancet 1983 Apr 2;1(8327):753-7.

Authors' abstract: Voluntary reporting of vaccine reactions was intensified in a single large region for 7 years. Anaphylaxis and collapse, convulsion, and neurological disorder were reported most frequently after diphtheria/-tetanus/pertussis (DTP). The greater frequency of recorded reactions after DTP than after DT could have been due to bias caused by the adverse publicity accorded to pertussis vaccine, since no major difference was found when the immunization histories of children admitted to hospital with such conditions were compared. No convincing evidence that DTP caused major neurological damage emerged from this large and lengthy study.

Pyrexia After Diphtheria/Tetanus/Pertussis and Diphtheria/Tetanus Vaccines

P.A. Waight, T.M. Pollock, E. Miller and E.M. Coleman. Arch Dis Child 1983 Nov;58(11):921-3.

Authors' abstract: The temperatures of 587 children were taken before and after diphtheria/tetanus/pertussis (DTP) or diphtheria/tetanus (DT) vaccine. Only slight temperature increases were found but these were notably more frequent after plain than adsorbed DTP vaccine preparations and the frequency increased with each successive dose.

DTP-Associated Reactions: An Analysis by Injection Site, Manufacturer, Prior Reactions and Dose

L.J. Baraff, C.L. Cody and J.D. Cherry. Pediatrics 1984 Jan;73(1):31-6.

Authors' abstract: Local and less serious systemic reactions are frequent following immunization with diphtheria-tetanus-pertussis (DTP) vaccine. The effects of injection site, manufacturer, previous reactions, and dosage reduction upon subsequent reactions to DTP immunization were investigated. Local reactions, notably pain and swelling, were less common when the immunization was given in the buttocks than in the thigh. No injection site was consistently associated with lower systemic reaction rates. There was no significant difference in the rate of more serious reactions by vaccine manufacturer. Differences in rates of less serious reactions by manufacturer were observed but seemed to be related to vaccine lot differences rather than the specific vaccines. In a

subset of 772 children, in whom data regarding sequential reactions were available, it was noted that all three reactions investigated—local redness, temperature ≥39° C, and persistent crying longer than one-half hour—were two to three times more frequent on a subsequent immunization when present on a prior vaccination than if not present on a prior vaccination. One hundred children received a half dose of DTP vaccine because of a less serious reaction associated with prior immunization. In all instances, they had significantly less serious local reactions as well as notable differences in temperature, drowsiness, and persistent crying.

Diphtheria

Population Studies of Diphtheria Immunity Using Antitoxin Radioimmunoassay

M.A. Menser and J.R. Hudson. J Hyg (Lond) 1984 Feb;92(1):1-7.

Authors' abstract: A quantitative method for testing serum diphtheria antitoxin levels was set up using a diphtheria antitoxin radioimmunoassay (RIA). The results of this RIA correlated well with the Schick test in 554 subjects and with intradermal neutralization tests in guinea-pigs in a small group of subjects. The RIA was suitable for use on blood collected by fingerprick on to a disc of standard chromatography paper. These discs could be stored at room temperature for at least 1 month. If storage for more than 6 months was required −20° C was found to be better. Experience with this RIA in a total of 2349 subjects indicated that it is more accurate, rapid and less costly than Schick testing. The RIA should prove to be the preferred method for testing diphtheria immunity in population surveys.

Studies on the Molecular Epidemiology of Diphtheria

A.M. Pappenheimer, Jr. and J.R. Murphy. Lancet 1983 Oct 22;2(8356):923-6.

Authors' abstract: DNA was extracted from toxigenic and nontoxigenic (tox+ and tox-) diphtheria bacilli isolated during a carrier survey that followed recovery of a tox+ *Corynebacterium diphtheriae* mitis from a baby with membranous tonsillitis. The electrophoretic gel patterns of restriction enzyme digests were indistinguishable from one another. They were, however, readily distinguishable from similar gels of DNAs extracted from diphtheria bacilli associated with outbreaks elsewhere. Hybridization of a labelled nick-translated corynephage-beta c-DNA probe to nitrocellulose blots of these gels occurred only to blots from tox+ strains. Other hybridization studies showed that all of seven strains, each isolated from a diphtheria case or carrier in a different part of the world, carried a prophage with DNA closely related to phage beta tox+. When an individual carrying a tox+ diphtheria bacillus arrives in an immunized community, spread of the tox gene to other individuals may be via phage conversion of tox- *C. diphtheriae* already prevalent among the nasopharyngeal bacterial flora of the local populace, rather than by colonization with the tox+ strain itself.

Circulation of the Causative Agent of Diphtheria in Immune Collectives (Russian)

N.L. Sukhorukova, V.V. Cherkasova, M.P. Korzhenkova and G.I. Kostiuchenko. Zh Mikrobiol Epidemiol Immunobiol 1983 Aug;(8):71-4.

English summary: Prolonged observations on the spread of toxigenic *C. diphtheriae* carriership, made during a school year in 12 groups of immune children (3809 children), showed that the penetration of diphtherial infection could give rise to the outbreak of bacterial carriership, its level being as high as 20.9-35.1% of the total number of children in the group. The spread of bacterial carriership occurred during the first months after the penetration of the infection, achieving its peak, then followed the subsidence of the infection in the focus. Though some children in the group persistently released *C. diphtheriae*, almost no new cases of carriership were registered in spring. The highest spread of carriership (55.6-73%) was revealed in the first forms of boarding schools despite a higher level of antitoxic immunity in these children. Cases of the spontaneous cessation of carriership were observed. The spread and subsidence of carriership were determined by the presence or absence of a susceptible contingent. Tests on guinea pigs, carried out in the course of this study to determine the toxigenicity of *C. diphtheriae*, showed its variability.

Results of Conducting an Epidemiological Survey of Diphtheria in 21 Territories of the RSFSR (Russian)

N.L. Sukhorukova, S.D. Gimpelevich, L.A. Favorova, S.S. Markina and V.V. Cherkasova. Zh Mikrobiol Epidemiol Immunobiol 1983 Nov;(11):95-8.

English summary: As the result of an epidemiological survey of diphtherial infection, carried out in conformity with the unified methodological recommendations in 21 regions of the RSFSR during 1980-1981, the expediency of such an experiment was established. Immunity to diphtheria in children aged up to 14 years was high: children with negative Schick tests constituted 96.9-99.1% of the total tested. No biological changes in *Corynebacterium diphtheriae* occurred during the term of observation. Toxigenic *C. diphtheriae* showed a high level of pathogenicity. The epidemiological survey contributed to a more thorough detection of diphtheria patients and carriers releasing toxigenic *C. diphtheriae*. The quality of clinical

bacteriological diagnosis improved. In rare cases angina with the concomitant carriership of toxigenic *C. diphtheriae* could be diagnosed with the indispensable serological examination of the patients by Jensen's method.

Survey on *Corynebacterium diphtheriae* Carriers and Susceptibility to Schick's Toxin in Diphtheria Contacts (Spanish)

S.A. Nogueira, L.C. Formiga and P.F.A. Lopez. Rev Latinoam Microbiol 1982 Oct-Dec;24(4):221-6.

English summary: Contacts of 30 index cases of diphtheria and 30 control families, living in similar environmental conditions, were examined in order to discover *C. diphtheriae* carriers.

A high carrier rate (14.2%) was observed in the 176 contacts of the index cases examined. 72% of the isolated *C. diphtheriae* strains were toxinogenic. A great number of these carriers were below 15 years old (67.8%). Among the 143 controls examined, 2.1% were *C. diphtheriae* carriers. Only non-virulent *C. diphtheriae* strains were isolated from this group.

A high degree of immunity to diphtheria was found among the contacts (81.2%) and controls (81.9%), based on the results of Schick and Moloney tests. This high percentage probably shows the importance of subclinical infections in the acquisition of natural immunity to the disease in our community. Two hundred twenty-two of 319 persons (69.6%) denied any previous vaccination against diphtheria. Lack of vaccination, in 72.8% of these cases, was attributed mainly to absence of basic information in the population about active immunization's protective effects.

Pertussis

Treatment of Whooping Cough: The Facts

J. Broomhall and A. Herxheimer. Arch Dis Child 1984 Feb;59(2):185-7.

From authors' discussion: Apart from drug treatment there has been little research into any aspect of the management of children with whooping cough. [Authors discuss current drug treatments for pertussis, including antibiotics, corticosteroids, salbutamol, antitussives and antispasmodics, sedation, and some therapeutic relics.] Treatment of whooping cough should aim to reduce mortality, the incidence of complications, and the severity of symptoms: it should shorten the length of the illness and prevent spread. Current treatment is largely based on the traditions and clinical experience of past generations and urgently needs scientific study. A logical starting point for investigation would be to set up a systematic confidential inquiry into all deaths from pertussis in the recent epidemic. This should establish the risk factors upon which treatment and prevention should focus. Further investigation of the pathophysiology of whooping cough by modern techniques will allow a more logical approach to drug treatment. Good clinical trials should be set up to distinguish valuable treatments from the others.

Serum IgA Antibody to *Bordetella pertussis* as an Indicator of Infection

J. Nagel and E.J. Poot-Scholtens. J Med Microbiol 1983 Nov;16(4):417-26.

Authors' abstract: The levels of pertussis-specific IgA antibodies in sera from vaccinees and from children with *Bordetella pertussis* infection were compared by an enzyme-linked immunosorbent assay (ELISA). Serum IgA antibodies were produced only after natural contact with the pathogen and, therefore, their presence can be used as an indicator of infection. However, in view of the relatively long interval between infection and the appearance of antibodies, and the prolonged antibody response, their presence cannot be used as proof of recent infection. The finding of these antibodies in a high percentage of the normal adult population may indicate a constant circulation of *B. pertussis* without symptoms of disease.

Adherence of *Bordetella pertussis* to Human Respiratory Epithelial Cells

E.I. Tuomanen and J.O. Hendley. J Infect Dis 1983 Jul;148(1):125-30.

Authors' abstract: Adherence of *Bordetella pertussis* to ciliated respiratory tract mucosa is important in the pathogenesis of whooping cough. The adherence of *B. pertussis* to human respiratory epithelial cells was investigated using cells obtained by brushing at bronchoscopy. *B. pertussis* attached exclusively to the ciliary tufts of ciliated cells. A mean ± SEM of 5.0 ± 0.3 organisms attached per cell when bacteria in a concentration of 2 X 10^9/ml were incubated with ciliated cells. Organisms examined by electron microscopy were found to adhere to the cilia both by direct apposition and by filaments coursing between bacteria and cilia. The specificity of the adherence of *B. pertussis* to ciliary tufts may explain the unique ability of this organism to infect the human tracheobronchial mucosa.

Distribution of Immunity to Pertussis in the Population of England and Wales

P.E. Fine and J.A. Clarkson. J Hyg (Lond) 1984 Feb;92(1):21-36.

Authors' abstract: This paper presents three different methods of estimating the number and age distribution of individuals susceptible to pertussis in England and Wales. The first approach is an extrapolation from data in the prevaccine era, the second is based upon theoretical consideration of the transmission dynamics of pertussis,

and the third is a detailed cohort analysis of available notification and vaccination data. Each of these analyses suggests that the total number of people susceptible to pertussis infection in England and Wales has remained at 3-4 million for the past 40 years, despite the increase and changes in numbers vaccinated. The effect of vaccination has been to reduce the incidence of infection and disease, but not to reduce the number of susceptibles. These findings, which are consistent with 'mass action theory', could be tested by an appropriately designed seroepidemiological survey.

Severity of Whooping Cough in England Before and After the Decline in Pertussis Immunization

T.M. Pollock, E. Miller and J. Lobb. Arch Dis Child 1984 Feb;59(2):162-5.

Authors' abstract: Since the decline of pertussis immunization, hospital admission and death rates from whooping cough have fallen unexpectedly. Although this might be taken to indicate that the disease is becoming less severe, a comparison of admissions and deaths in England and Wales before and after the decline in immunization suggests that several factors other than disease severity—a shift in the social class distribution of the disease, an increase in the proportion of milder cases notified, and improved care—were responsible for this. The severity of attacks and the complication rates in children admitted to hospital were virtually unchanged. Very young infants, those from disadvantaged families, and children with chronic illness were at greatest risk.

Intrafamilial Spread of Pertussis

J. Mertsola, O. Ruuskanen, E. Eerola and M.K. Viljanen. J Pediatr 1983 Sep;103(3):359-63.

Authors' abstract: Intrafamilial spread of pertussis was evaluated in 21 families (97 individuals) of patients with whooping cough diagnosed by culture or by ELISA serology. During follow-up (average six months), an infectivity rate of 83% was established by an ELISA within these families. However, 46% of the secondary cases were asymptomatic. Most of the asymptomatic cases were in adults or vaccinated children. Unvaccinated infants had classic whooping cough and were exposed to pertussis by their vaccinated siblings or parents. The incidence of classic symptoms of pertussis decreased with age, and atypical pertussis was usually culture negative but rapidly diagnosed by measurement of the IgM- and IgA-class antibodies by ELISA.

Bordetella pertussis Isolation in General Practice: 1977-1979 Whooping Cough Epidemic in West Glamorgan

W. Kwantes, D.H. Joynson and W.O. Williams. J Hyg (Lond) 1983 Apr;90(2):149-58.

Authors' abstract: Some of the factors influencing the isolation rate of *Bordetella pertussis* during a whooping cough epidemic in West Glamorgan, Wales, are reported. The organism was isolated from 39% of patients with clinical whooping cough, pernasal swabbing being much more successful than cough plates. Isolation rates were increased in the non-immunized, particularly in the first year of life. Erythromycin and co-trimoxazole significantly reduced the isolation rate of *B. pertussis* but this did not occur with penicillin. In this study 20% of patients were culture positive 6 weeks after the onset of their infection. It is suggested that the Department of Health and Social Security recommendation of a minimum period of three weeks exclusion of children from school is inadequate. During the epidemic, the proportion of strains of *B. pertussis* containing antigen 2 more than doubled.

Current Status of Pertussis and Pertussis Vaccination in Finland

J. Mertsola, M.K. Viljanen and O. Ruuskanen. Ann Clin Res 1982 Dec;14(5-6):253-9.

Authors' abstract: The pertussis vaccination program was started in Finland in 1952. Since then the incidence of the disease has decreased. No major epidemics have occurred during the last two decades. The majority of the patients with pertussis are children of school age. Their disease is characterized by prolonged cough without whooping and it is difficult to diagnose. The patients with atypical pertussis are, however, the major reservoir for transmission of the disease to young infants, in whom it can be serious. Recently developed ELISA for measuring antipertussis IgM and IgA antibodies is a valuable aid in the diagnosis of these cases. Pertussis vaccination has been a subject of considerable controversy in recent years. The vaccine used in Finland has proved to be safe and effective. This observation emphasizes the need for careful comparison of the vaccines used in different countries.

Development of a Pertussis Component Vaccine in Japan

Y. Sato, M. Kimura and H. Fukumi. Lancet 1984 Jan 21;1(8369):122-6.

Authors' abstract: Antibodies against two physicochemically purified hemagglutinins (HAs) of *Bordetella pertussis* (filamentous HA and leukocytosis-promoting-factor HA) protect laboratory animals from pertussis. A vaccine containing these two HAs was prepared and tested in trials involving about 5000 children. Culture supernatant of *Bordetella pertussis*, phase I, was

treated with ammonium sulphate, and a crude extract of the HAs was extracted from the precipitate by the use of concentrated sodium chloride. This crude extract was fractionated by sucrose density gradient centrifugation to obtain an HA preparation practically free of endotoxin. The HA preparation was treated with formalin to destroy its ability to induce leukocytosis and to cause histamine sensitization. Aluminum hydroxide was added to the preparation as an adjuvant. The component vaccine is not only potent as judged by the mouse test but is also less than one-tenth as toxic as whole-cell vaccine as judged by leukocytosis promotion, histamine sensitization, and endotoxicity tests. Field trials showed that component vaccine was as effective as and produced less side-effects than did conventional whole-cell vaccine. The vaccine has been used for mass immunization in Japan since the autumn of 1981.

Serological Response to Filamentous Hemagglutinin and Lymphocytosis-Promoting Toxin of *Bordetella pertussis*

D.G. Burstyn, L.J. Baraff, M.S. Peppler, R.D. Leake, J. St. Geme, Jr. and C.R. Manclark. Infect Immun 1983 Sep;41(3):1150-6.

Authors' abstract: Serum antibody responses to the filamentous hemagglutinin and the lymphocytosis-promoting toxin of *Bordetella pertussis* after vaccination with diphtheria and tetanus toxoids and pertussis vaccine, adsorbed, were assayed by using the enzyme-linked immunosorbent assay. The effect of early immunization, during the first week of life, on the antibody response also was determined. After vaccination, immunoglobulin G (IgG) and IgM directed against both the filamentous hemagglutinin and the lymphocytosis-promoting toxin were detected. Generally, antibody titers increased with subsequent injections and the age of the children. Maternal antibodies against filamentous hemagglutinin and lymphocytosis-promoting toxin were detected in cord blood. The ability of an infant to produce serum IgG anti-lymphocytosis-promoting toxin after vaccination with pertussis vaccine was inversely related to the cord blood serum IgG anti-lymphocytosis-promoting toxin titer at birth. A good antibody response was observed in infants with low cord blood titers, and a poor antibody response was seen in infants with high cord blood values. The IgM anti-lymphocytosis-promoting toxin response was good in groups with both low and high cord blood titer, with no significant difference observed between the two groups. No IgA anti-lymphocytosis-promoting toxin or IgA anti-filamentous hemagglutinin titers were observed in vaccines. IgA antibodies were observed in convalescent sera from two adults and may be presumptive evidence of infection with *B. pertussis*.

Antigens in Whooping Cough Vaccine and Antibody Levels Induced by Vaccination of Children

L.A. Ashworth, A. Robinson, L.I. Irons, C.P. Morgan and D. Isaacs. Lancet 1983 Oct 15;2(8355):878-81.

Authors' abstract: The content of 3 antigens—filamentous hemagglutinin, lymphocytosis-promoting factor, and serotype-specific agglutinogens (fimbriae)—was determined in the current UK whole-cell whooping cough vaccine. Antibodies to these antigens and to outer membrane proteins and lipopolysaccharide of *Bordetella pertussis* were measured in the serum of unvaccinated children and children who had received 1, 2, or 3 doses of the vaccine. Children who had received one dose of vaccine had varied low antibody titers. Children who had received two or three doses had significantly higher antibody titers to all the antigens tested, as did some unvaccinated children with no history of whooping cough. This study shows that filamentous hemagglutinin, lymphocytosis promoting factor, and outer membrane proteins are immunogenic constituents of the whole-cell vaccine. Their inclusion in a subcellular vaccine would not involve novel antigens.

Pertussis: Should We Immunize Neurologically Disabled and Developmentally Delayed Children?

R.N. Miles and G.P. Hosking. Br Med J [Clin Res] 1983 Jul 30;287(6388):318-20.

Authors' abstract: A total of 400 children with neurological disorders were studied to ascertain whether they had been immunized against pertussis, the reasons for non-immunization, and the "validity" of these reasons, as judged by interpretation of the recommendations of the Department of Health and Social Security. The results for this group were compared with those for a group of 400 age-matched controls. The study group had a significantly lower rate of immunization than controls ($p<0.01$); rates for both groups fell sharply after 1975. A total of 192 study patients and 186 controls were not immunized. Those children with cerebral palsy had the lowest rate of immunization (19%) and the highest number of valid reasons for non-immunization (63%). Pediatricians apparently advised against immunization in 61 (32%) of the index group but in only four (2%) of the controls. The risk of serious neurological handicap after pertussis immunization is small and there is little evidence to support the view that underlying neurological disease predisposes a child to increased risk. The advice currently given by pediatricians may need to be reconsidered.

Immunization Against Whooping Cough: A Neuropathological Review

J.A. Corsellis, I. Janota and A.K. Marshall. Neuropathol Appl Neurobiol 1983 Jul-Aug;9(4):261-70.

Authors' abstract: The neuropathological aspects of vaccination against pertussis have been analyzed. This has been done partly by considering the previous literature and partly by searching for data on any child whose death since 1960 has been thought to have a possible relationship to the vaccination. Twenty-nine in due course were identified on whom a post-mortem examination had been made. Eighteen had died within 3 weeks of inoculation—the remaining eleven had survived the initial illness but had remained retarded, epileptic and disabled. Although a variety of cerebral abnormalities were found, neither those recorded in the present study nor those abstracted from previous case reports, have demonstrated a recurring pattern of inflammatory or other damage which could be accepted as a specific reaction to immunization against whooping cough. Those reactive changes that were occasionally found appear to be indistinguishable from those seen in many other infantile encephalopathies occurring as the result of a hypoxic/ischemic state supervening on a complex of respiratory complications, fever and convulsions.

Infantile Spasms and Pertussis Immunization

M.H. Bellman, E.M. Ross and D.L. Miller. Lancet 1983 May 7;1(8332):1031-4.

Authors' abstract: The possible roles of pertussis immunization and of other factors in the etiology of infantile spasms were investigated by analysis of 269 cases reported to the National Childhood Encephalopathy Study. In 34% of the cases an antecedent factor which may have caused infantile spasms was identified; the commonest of these were perinatal hypoxia (38 cases) and tuberous sclerosis (16 cases). Case-control analyses showed no significant association between infantile spasms and pertussis immunization in the 28 days before onset. There was, however, some clustering of cases immunized with either diphtheria-tetanus-pertussis or diphtheria-tetanus vaccines in the 7 days before onset. The excess compared with controls was compensated for by a corresponding deficit over the remaining period up to 28 days. It is suggested that these vaccines do not cause infantile spasms but may trigger their onset in those children in whom the disorder is destined to develop.

Tetanus

Neonatal Tetanus: Mode of Infection, Prevalence, and Prevention in Southern Sudan

A.W. Woodruff, J. Grant, E.A. El Bashir, E.I. Baya, A.Z. Yugusuk and A. El Suni. Lancet 1984 Feb 18;1(8373):378-9.

Authors' abstract: Neonatal tetanus affects 1 in every 82 and kills 1 in every 110 infants born in the town of Juba, southern Sudan. It is also an important cause of death in adult life both in southern Sudan and in many other regions of the developing world. One vehicle of infection could be the fine string-like roots used to tie the cord. To prevent neonatal tetanus, governments and aid-giving agencies should distribute to women and midwives kits containing a sterile blade, a sterile ligature, two or three sterile adhesive dressings for the umbilical stump, and two or three sterile swabs.

The Dynamics of Tetanus Epidemiology and Control in Rural Uttar Pradesh Studied Through Computer Simulation

M. Sharma and P.D. Sharma. Soc Sci Med 1984;18(4):303-13.

Authors' abstract: An epidemiological model is constructed for tetanus. The assumptions as well as the steps involved in the construction of the model, are detailed. The impact of alternate immunization strategies to control tetanus in rural Uttar Pradesh is studied using this model. The quantification of the expected decline in incidence and mortality over 30 years, for different control strategies, provides the health planner with valuable information. It is seen that the incidence of tetanus neonatorum and tetanus in adults, as well as deaths due to tetanus, progressively decreases as the level of coverage is increased. The most marked reduction is seen over the initial period of intervention. Mass immunization of the total population, or of just the females in the reproductive age group, leads to temporary decline in the endemic level. Such models are useful for planning in the health sector in India since they can be constructed with the limited information available.

Tetanus and Diphtheria Immunity in an Elderly Population in Los Angeles County

B.P. Weiss, M.A. Strassburg and J.C. Feeley. Am J Public Health 1983 Jul;73(7):802-4.

Authors' abstract: Fifty-four per cent of 246 subjects attending senior citizen centers (mean age 69), and 29 per cent of 111 convalescent hospital subjects (mean age 82) had protective levels of tetanus antitoxin ($\geq$0.01 units/ml). Age-specific immunity levels were lower for females than males, and generally decreased with age.

Forty-eight and one-half per cent of the senior citizen center subjects and 55.9 per cent of the convalescent hospital subjects had protective levels of diphtheria antitoxin (≥0.01 units/ml).

Tetanus in Victoria, 1957-1980. Review of 106 Patients Managed in One Hospital

H.F. Newton-John. Med J Aust 1984 Feb 18;140(4): 194-200.

Author's abstract: The records of 106 patients with tetanus who received treatment in Fairfield Hospital, Melbourne, over a 24-year period were reviewed. There were 19 deaths, all before 1975, and mortality was highest in patients over 60 years of age. During the second half of the study period, very few young people with tetanus were admitted to hospital, whereas the admission rate of those over 40 years of age was constant. Sixty-four patients were known not to be immunized; 19 patients had received at least one prior dose of tetanus toxoid. Ninety-one patients had identifiable injuries, most of which were minor. Medical treatment for an injury was given to 43 patients; 35 of these received tetanus prophylaxis, but only eight received tetanus immunoglobulin. In the last six years of the survey, improved treatment techniques have helped to reduce the mortality from tetanus. The accumulated experience at Fairfield Hospital provides a basis for the proposal that all patients with tetanus in Victoria should be referred to one hospital for management.

Adequacy of Antitetanus Prophylaxis in Six Hospital Emergency Rooms

D.A. Brand, D. Acampora, L.D. Gottlieb, K.E. Glancy and W.H. Frazier. N Engl J Med 1983 Sep 15;309(11):636-40.

Authors' abstract: We studied the adequacy of antitetanus prophylaxis given to 620 patients with open soft-tissue injuries by 169 physicians in six hospital emergency rooms. Twenty-three per cent of the patients were treated incorrectly (6 per cent were undertreated and 17 per cent were overtreated) with tetanus toxoid or human tetanus immunoglobulin. Undertreatment ranged from 4 to 11 per cent, and overtreatment from 5 to 38 per cent at the different hospitals ($p<0.01$). Patients at highest risk for tetanus (those with tetanus-prone wounds who had never been given a complete initial course of immunizations) had the lowest likelihood (27 per cent) of receiving correct antitetanus treatment. By following an immunization protocol based on time since injury, mechanism of injury, estimated bacterial contamination, presence of devitalized tissue, wound depth, and past immunizations, physicians can better protect the population against tetanus while lowering the risk of adverse drug reactions and not increasing the cost of care.

Infectious Diseases and Aging: Immunologic Perspectives

J.M. Felser and M.J. Raff. J Am Geriatr Soc 1983 Dec;31(12):802-7.

Authors' abstract: Four theories of aging provide a basis for understanding both the aging process and the primary alterations in host defenses that may occur with age. The immunologic theory of aging may be especially important in this regard, since immunologic defects may be responsible for many manifestations of aging, and a decline in immune function may also underlie the increased susceptibility of the aged to infection. However, multiple factors are probably responsible for the aging process and for changes in host defenses. Although several studies attempting to enhance the immune response of elderly persons and perhaps extend lifespan are in progress, no factor at present appears to be as important in this regard as three underutilized immunizations for influenza, pneumococcal infection, and tetanus.

Response to Tetanus Immunization in Onchocerciasis Patients

A. Prost, M. Schlumberger and M.T. Fayet. Ann Trop Med Parasitol 1983 Feb;77(1):83-5.

Authors' abstract: Fifty-five people were examined for tetanus antitoxin level two months after immunization with a single 0.5 ml dose of concentrated tetanus toxoid vaccine; only 7.1% of patients infected with onchocerciasis became immunized, whereas 44.5% were immunized in the control group. These results are consistent with previous observations of a reduced level of both cell-mediated and humoral immunity in patients heavily infected with parasitic diseases, especially onchocerciasis. This study raises doubts about the efficacy of immunization in young adult age groups and re-emphasizes the need for immunization in infancy.

Timing of Antenatal Tetanus Immunization for Effective Protection of the Neonate

S.T. Chen, G. Edsall, M.M. Peel and T.A. Sinnathuray. Bull WHO 1983;61(1):159-165.

Authors' abstract: A study was undertaken to determine the relationship between the timing of maternal immunization with a commercially available adsorbed tetanus toxoid and the presence of protective antitoxin in cord blood. Women at various stages of gestation were given one or two doses of 20 IU of toxoid, and the maternal and cord sera collected at delivery were assayed for tetanus antitoxin by the indirect hemugglutination and toxin neutralization techniques.

Results indicated that the first injection of a two-dose schedule should be given at least 60 days, and preferably 90 days or more before delivery, with the second injection 20 days or more before delivery. The single-dose

schedule conferred no significant protection when given less than 70 days before delivery; beyond 70 days, protection rates improved, but there were too few subjects to allow any definite conclusions to be made.

Cord and maternal antitoxin titers differed by not more than one twofold dilution for almost all of the individual paired sera. A cord/maternal antitoxin ratio of 2 was more likely to occur with increasing time between the second injection and delivery.

Transplacental Immunization of the Human Fetus to Tetanus by Immunization of the Mother

T.J. Gill, 3d., C.F. Repetti, L.A. Metlay, B.S. Rabin, F.H. Taylor, D.S. Thompson and A.L. Cortese. J Clin Invest 1983 Sep;72(3):987-96.

Authors' abstract: Experimental studies in rats showed that immunization of the pregnant female led to the transplacental immunization of her fetuses. The possibility that this also occurred in humans was explored by immunizing 42 pregnant women with tetanus toxoid (2.5 or 5 Lf) in the fifth and eighth months of pregnancy and comparing the immune responses of their offspring with the responses of the offspring of 25 unimmunized mothers. Only the offspring of the immunized mothers were sensitized to tetanus. IgM antitetanus antibodies were in their blood before immunization with diphtheria, pertussis, tetanus vaccine (DTP), they had a more rapid ($p<0.01$) response to DTP immunization, and they were still highly sensitized ($p<0.01$) to tetanus 13 months after birth. In addition, pregnancy had no immunosuppressive effect ($p<0.05$) on the responses of the mothers to tetanus toxoid. Thus, transplacental immunization occurs in humans; it enhances the response of the offspring to subsequent immunization, and it could be used to circumvent the necessity for immunization in early neonatal life.

Production of Human Antitetanus Antibodies by Hybridomas (French)

H.J. Garchon, A. Blancher, F. Champommier, A. Blanchard de Vaucouleurs, J.F. Bach and J. Hainaut. Rev Fr Transfus Immunohematol 1983 Apr;26(2):147-51.

English summary: Peripheral blood lymphocytes from healthy people recently immunized against tetanus toxoid (TT) were fused with human malignant B-cell lines or mouse myeloma cells (X63 Ag8.653) in an attempt to establish stable B cell hybridomas secreting anti TT antibodies. Human-human fusion experiments were not successful. In contrast, the five heterospecific fusion experiments yielded between 60 and 100% of wells that contained growing hybrids. Five of these hybrids repeatedly secreted anti-TT antibodies. One of the hybrids was cloned and secreted 10-20 micrograms/ml of human IgM, lambda anti-TT antibody. Heterospecific hybridization thus appears as an interesting method to obtain human monoclonal antibodies, allowing the study of their properties.

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OTHER VACCINE-PREVENTABLE DISEASES

General

Immunogenicity of a *Hemophilus influenzae* Type B Vaccine in Combination with Diphtheria-Pertussis-Tetanus Vaccine in Infants

J.L. Coulehan, C. Hallowell, R.H. Michaels, T.K. Welty, N. Lui and J.S. Kuo. J Infect Dis 1983 Sep;148(3):530-4.

Authors' abstract: Seventy-eight Navajo infants (one to two months of age) were randomly assigned to one of two vaccination groups: one group (40 infants) was scheduled to receive three doses of diphtheria-pertussis-tetanus (DPT) vaccine and the other (38 infants) to receive DPT combined with *Hemophilus influenzae* type b polyribosyl-ribitol phosphate (DPT + PRP vaccine). In the latter vaccine, pertussis antigen served as an adjuvant for PRP. Sixty-seven infants (37 who received DPT vaccine and 30 who received DPT + PRP vaccine) completed the protocol. Local and systemic reactions were equally frequent in the two groups. Fifty percent of the infants who received DPT + PRP vaccine had definite antibody responses to PRP after three doses, and 13% had possible responses. Of the infants who received DPT vaccine, 14% and 8% had definite and possible responses, respectively; three of five infants with definite responses were infected with *H. influenzae* type b or cross-reacting organisms, as determined by pharyngeal cultures. The immune response did not appear to be suppressed by the presence of maternal antibody.

Neutralizing Antibody Responses to Japanese Encephalitis Vaccine in Children

R.F. Juang, Y. Okuno, T. Fukunaga, M. Tadano, K. Fukai, K. Baba, N. Tsuda, A. Yamada, and H. Yabuuchi. Biken J 1983 Mar;26(1):25-34.

Authors' abstract: Two shots of the current Japanese encephalitis (JE) vaccine were given to children and their immune responses to the Nakayama strain (the vaccine strain) and two wild strains (JaGAr-01 and E-50) of JE virus were examined by neutralizing (N) antibody titrations. Seventy vaccinees had no N antibody to JE virus before the first vaccination and were bled one month after the second vaccination. The N antibody responses to the JaGAr-01 and E-50 strains were found to be similar and to be less than that to the Nakayama strain after the second vaccination: the geometric mean titers (GMT) of N antibodies to the JaGAr-01 and E-50 strains (as logarithms) were 1.87 and 1.75, respectively, while the GMT to the Nakayama strain was 2.89. The seroconversion rates to the Nakayama, JaGAr-01 and E-50 strains were 70/70 (100%), 69/70 (99%) and 68/70 (97%), respectively, after the second vaccination. Twenty-seven of the 70 vaccinees were also bled before the second vaccination. Most of them showed a considerably high N antibody response against the Nakayama strain and only one vaccinee failed to show seroconversion after the first vaccination. However, the antibody response to the E-50 strain appeared to be rather low and 9 of 25 vaccinees did not show any seroconversion. Similarly 3 of 25 failed to show any seroconversion against the JaGAr-01 strain. These results indicate that at the initial immunization two shots, at least, of the current JE vaccine are necessary to stimulate effective immune responses to wild strains of JE virus.

Epidemiologic Background for the Need of Rotavirus Vaccine in Finland. Preliminary Experience of RIT 4237 Strain of Live Attenuated Rotavirus Vaccine in Adults

T. Vesikari, M. Maki, and E. Isolauri. Dev Biol Stand 1983;53:229-36.

Authors' abstract: Epidemiologic evidence from Finland indicates a dramatic change in the seasonal pattern of acute diarrhea over the past 30 years. While in the 1950's the majority of cases occurred in late summer the seasonal peak in the 1970's was in winter and spring, coinciding with the prevalence of rotavirus infections. It is not possible to determine retrospectively the etiologic agents involved in the summer diarrhea, but EPEC may have been one of them, as EPEC are quite rare in Finland

today compared to the 1950's. Another change over the time period is a shift in the age distribution of acute diarrhea from neonates towards older infants. Rotavirus is today associated with approximately 50% of the cases of acute diarrhea in children in Finland. Based on experience in one Central Hospital it was estimated that the treatment of rotavirus infections may require some 7300 hospital days in Finland annually, which figure is comparable to that of mumps. As a recent cost-benefit analysis in Finland indicated that a mumps vaccination program would be economically quite efficacious, the same could be assumed to be true for rotavirus vaccination, provided that an effective and safe vaccine was available. In a preliminary trial of RIT 4237 strain of live attenuated rotavirus vaccine in 20 healthy adult volunteers no clinical symptoms and no excretion of vaccine virus were observed. Rotavirus ELISA antibody booster response was found in 1/20 vaccinees.

Immunogenicity and Safety of Live Oral Attenuated Bovine Rotavirus Vaccine Strain RIT 4237 in Adults and Young Children

T. Vesikari, E. Isolauri, A. Delem, E. D'Hondt, F.E. Andre and G. Zissis. Lancet 1983 Oct 8;2(8354):807-11.

Authors' abstract: A candidate oral live rotavirus vaccine, strain RIT 4237, of bovine origin, was tested for immunogenicity and safety in man. In adults the vaccine did not cause clinical symptoms, and a booster response in rotavirus serum antibodies was seen in 2/20 subjects. In seronegative young children one oral dose induced seroconversion to homologous virus in 15/17 (88%) children seronegative by enzyme immunoassay and in 13/19 (68%) children seronegative by a neutralization assay. The vaccine did not produce gastrointestinal or constitutional symptoms in the children, nor did it cause rotavirus excretion in the stools. The results suggest that the RIT 4237 strain is a promising candidate for a vaccine against human rotavirus, and the vaccine-induced immunity against natural human rotavirus infection should be evaluated in future trials.

Cholera

Differences in Cross-Protection in Rats Immunized with the B Subunits of Cholera Toxin and *Escherichia coli* Heat-Labile Toxin

F.A. Klipstein, R.F. Engert, J.D. Clements and R.A. Houghten. Infect Immun 1984 Mar;43(3):811-6.

Authors' abstract: Although cholera toxin (CT), *Escherichia coli* heat-labile toxin (LT), and their B subunits are known to be immunologically related, the ability of each to raise an antitoxin response that provides equally strong cross-protection against active challenge with pure heterologous toxin has not been examined previously. We immunized rats with pure preparations of the B subunits of human LT, porcine LT, and CT. Immunization with either of the LT B subunits raised greater than or equal to fourfold increases in specific mucosal immunoglobulin A antitoxin titers to homologous and heterologous LT and CT B subunits, thereby providing strong protection against active challenge in ligated ileal loops with all three respective holotoxins and with a viable LT-producing *E. coli* strain. In contrast, immunization with the CT B subunit raised a greater than or equal to fourfold increase in antitoxin titers only to itself and provided strong protection only against challenge with the CT holotoxin. Conjugation of the CT B subunit with the *E. coli* heat-stable toxin by the carbodiimide reaction yielded a cross-linked immunogen with equal antigenicity for both components; immunization with this conjugate raised greater than or equal to fourfold increases in antitoxin titers to both components, but it provided significant protection only against challenge with a viable heat-stable toxin-producing *E. coli* strain and not to an LT-producing *E. coli* strain. These observations indicate that immunization with the LT B subunits raises a heterologous antitoxin response that extends to the CT B subunit, thereby providing equally strong protection against LT and CT; however, immunization with the CT B subunit raises principally a homologous antitoxin response, so that this immunogen provides strong protection only against CT.

Evaluation in Humans of Attenuated *Vibrio cholerae* El Tor Ogawa Strain Texas Star-SR as a Live Oral Vaccine

M.M. Levine, R.E. Black, M.L. Clements, C. Lanata, S. Sears, T. Honda, C.R. Young and R.A. Finkelstein. Infect Immun 1984 Feb;43(2):515-22.

Authors' abstract: Texas Star-SR, an A- B+ mutant derived by nitrosoguanidine treatment from *Vibrio cholerae* El Tor Ogawa strain 3083, was fed to 68 volunteers as an oral vaccine in doses of 10^5 to 5 X 10^{10} organisms with $NaHCO_3$. Sixteen (24%) vaccinees experienced some loose stools (unrelated to vaccine dose), but in only one did the total stool volume exceed 1.0 liter. The vaccine strain was cultured from duodenal fluid of 35 of 46 (76%) persons who ingested doses of 10^8 organisms or greater. No A+ B+ toxinogenic revertants were found among 456 clinical isolates tested. Sixty-three vaccinees (93%) manifested seroconversions of vibriocidal antibody, whereas only 20 (29%) had significant rises in serum antitoxin titers. Paired intestinal fluids from 41 volunteers showed significant rises of secretory immunoglobulin A against lipopolysaccharide (29%), Ogawa outer membrane preparation (29%), and toxin (12%) antigens. In challenge studies with pathogenic *V. cholerae* El Tor Ogawa and El Tor Inaba, the attack rate in vaccinees (7 of 25) was significantly lower than in controls (18 of 25) (vaccine efficacy, 61%); furthermore, the diarrheal stool volume in vaccinees was significantly less than that in

controls ($p<0.01$). Texas Star-SR served as a prototype to investigate the concept of immunoprophylaxis by means of attenuated strains as oral vaccines. These observations provide an invaluable background for planning future studies with newly developed attenuated strains prepared by recombinant DNA techniques.

Sudden, Unexpected Death Following Typhoid-Cholera Vaccination

D.J.Pounder. Forensic Sci Int 1984 Jan;24(1):95-8.

Author's abstract: A previously healthy 33-year-old Australian male died suddenly and unexpectedly 8 hours after a typhoid-cholera vaccination. Such fatalities are extreme rarities and the present case is the first in which postmortem measurement of serum immunoglobulins has been undertaken. The clinical course and necropsy findings suggest that death was the result of a slowly evolving systemic anaphylactic reaction which terminated in hypotension and right heart failure. The deceased was probably atopic. The current recommendations for the vaccination of international travellers against typhoid and cholera are discussed.

Dental Caries

Induction and Delivery of Mucosal Immune Responses

A.J. Husband, M.L. Dunkley, R. Scicchitano and R.F. Sheldrake. J Dent Res 1984 Mar;63(3):465-9.

Authors' abstract: The oral cavity is relatively deficient in lymphoid tissue capable of directing the inductive and effector events required for effective mucosal IgA responses to local antigen. Recent evidence regarding a common mucosal immune system has raised new possibilities in immunization of mucosal surfaces. This review describes the role of the intestine in contributing to responses at distant mucosal sites and in particular emphasizes the immune potential of the intestine in determining the success of immunization strategies to control dental caries.

Hemophilus influenzae Infections

Efficacy of *Hemophilus influenzae* Type B Capsular Polysaccharide Vaccine on the Incidence of Epiglottitis and Meningitis

H. Peltola, M. Virtanen and P.H. Makela. Pathol Biol (Paris) 1983 Feb;31(2):141-3.

48,997 children of 3 months to 5 years were vaccinated with *Hemophilus influenzae* type b (Hib) capsular polysaccharide vaccine in a double blind study carried out in Finland in 1974. A clear-cut effect was obtained in the incidence of epiglottitis. The number of patients decreased 58% for three years when compared with the three-year-period before vaccination ($p<0.002$). On the other hand, the number of cases during the three years following vaccination was 65% less than during the next three year period ($p<0.001$). The efficacy implies an exceptionally strong herd immunity, because only 37.7% of the children in the area were vaccinated. Regarding meningitis, no herd immunity was observed but vaccination induced a highly significant ($p<0.001$) individual protection (2 cases in the specifically vaccinated versus 20 in the control group in four years' time), provided the vaccine was given at the age of 18 months or later. No efficacy was obtained before this age limit. It was calculated that approximately 90 per cent of cases of epiglottitis and 50 per cent of meningitis would be prevented with the vaccine currently available. Taking also into account the strong herd immunity tendency, vaccination is likely to offer even larger benefits.

Meningococcal Infections

Failure of Meningococcal Vaccination to Stop the Transmission of Meningococci in Nigerian Schoolboys

I.S. Blakebrough, B.M. Greenwood, H.C. Whittle, A.K. Bradley and H.M. Gilles. Ann Trop Med Parasitol 1983 Apr;77(2):175-8.

Authors' abstract: A combined group A and group C meningococcal polysaccharide vaccine was given to 438 Nigerian schoolboys shortly before an outbreak of group A meningococcal disease occurred in their school. Four months after vaccination the carriage rate of group A meningococci among vaccinated subjects (11%) was no different from that found among the controls (12%), although a good antibody response to both components of the vaccine was observed. One case of group A meningococcal disease was recorded amongst 438 vaccinated subjects while five cases occurred among 874 controls.

Effect of *Neisseria meningitidis* Group A Polysaccharide Vaccine on Nasopharyngeal Carrier Rates

A. Sivonen. J Infect 1981 Sep;3(3):266-72.

Author's summary: The effect of *Neisseria meningitidis* group A polysaccharide vaccine on nasopharyngeal carriage was studied in the Finnish Armed Forces during an epidemic of meningitidis caused by *N. meningitidis* group A. In 1974, half of all new recruits received the vaccine (16,458 vaccinated) when entering service. Nasopharyngeal swabs were cultured for *N. meningitidis* at this time and again four weeks later in a follow-up cohort of about 1200 men. Another set of 1101 samples were collected

and cultured seven to 16 weeks after entering service from recruits in all garrisons that had had cases of purulent meningitis. In most garrisons the carrier rates of group A *N. meningitidis* were low (average 12 per cent) or moderate (7 to 9 per cent) throughout the study without difference between the vaccinated and unvaccinated men. However, in three garrisons the carrier rates of group A strains were high (average 24 per cent) among those not vaccinated, and significantly lower (average 9 per cent) among group A vaccinees. Carriage of other, non-group A *N. meningitidis* was high, 75 per cent in all groups. Since group A strains were rare in men entering service (average 22 per cent in 1974), the group-specific inhibition of carriage by the vaccine was concluded to be due to its ability to prevent acquisition of group A strains in the nasopharynx.

Mumps

Clinical Appearance and Outcome in Mumps Encephalitis in Children

M. Koskiniemi, M. Donner and O. Pettay. Acta Paediatr Scand 1983 Jul;72(4):603-9.

Authors' abstract: Forty-one patients with mumps encephalitis examined at the Department of Pediatrics, University of Helsinki, during the period January 1, 1968, to December 31, 1980, were reviewed with special reference to clinical appearance and outcome. The ratio of males to females was 4:1 and the age range 1.2 to 13.7 years. The clinical findings were high fever (≥39° C in 83.0%), impairment of locomotion and balance (36.6%), seizures (24.4%), psychic disorders (22.0%), depressed level of consciousness (19.5%), vertigo (12.9%) and/or gastric pains (12.9%). One patient with congenital toxoplasma and cytomegalovirus infections died. On leaving the hospital eight were still ataxic, one of these was not able to speak and two had difficulties in concentration. One patient was transferred to another hospital because of psychosis. At the follow-up examination 4 to 24 months after the onset of the disease two patients were ataxic and seven suffered from behavioral disturbances. Electroencephalography (12.2% of all and 25% of examined patients) showed generalized slow wave disturbance at follow-up in six patients and borderline disturbances in eight.

Local T Cell Subsets in Mumps Meningitis

H. Nagai, T. Morishima, Y. Morishima, S. Isomura and S. Suzuki. Arch Dis Child 1983 Nov;58(11):927-8.

Authors' abstract: In the acute phase of mumps meningitis, more than 85% of the cells in cerebrospinal fluid (CSF) were OKT 3 positive, while 76% of the peripheral mononuclear cells (PMN) were OKT 3 positive. The ratio of OKT 4:8 positive cells in CSF was significantly lower than that in PMN, showing that suppressor/cytotoxic T cells had selectively accumulated in CSF. In addition, 58% of CSF cells were immune associated (Ia) positive, probably activated T cells.

Hemadsorption Immunosorbent Technique for Determination of Mumps Immunoglobulin M Antibody

J.T. van der Logt, F.W. Heessen, A.M. van Loon and J. van der Veen. J Clin Microbiol 1982 Jan;15(1):82-6.

Authors' abstract: We used hemadsorption immunosorbent technique (HIT) to detect mumps immunoglobulin M (IgM) antibody. IgM from human sera was adsorbed into anti-human IgM-coated wells in plates, and mumps-specific IgM was detected by adding mumps virus hemagglutinin and guinea pig erythrocytes consecutively. Specific IgM-positive sera showed hemadsorption, whereas negative sera showed hemagglutination. All 81 patients with current mumps infections tested showed mumps-specific IgM antibody, with titers ranging from 160 to 327,680. In most cases IgM antibody was already present on day 1 or 2 after the onset of illness. IgM antibody persisted for 6 to 10 weeks. Of 57 patients with acute respiratory illnesses caused by parainfluenza virus, 5 showed cross-reactions in the hemadsorption immunosorbent technique assay for mumps IgM. The hemadsorption immunosorbent technique assay is specific for the IgM class of antibody and avoids false-positive results due to rheumatoid factor. This test is an efficient and sensitive method for rapid and early diagnosis of mumps infections.

Virus-Specific Secretory IgA Antibodies as a Means of Rapid Diagnosis of Measles and Mumps Infection

M. Friedman, I. Hadari, V. Goldstein and I. Sarov. Isr J Med Sci 1983 Oct;19(10):881-4.

Authors' abstract: A highly sensitive solid-phase radioimmunoassay has been developed for the detection of virus-specific IgA antibodies in saliva obtained from infants and children. Serial saliva samples from infants and children under 3 years of age with acute measles or mumps infection, or after measles immunization, were examined for their content of virus-specific IgA antibodies. Virus-specific antibodies appeared transiently in the saliva in both illnesses and after immunization with live attenuated measles vaccine. The significance of this finding for rapid diagnosis of these infections without the necessity of drawing a blood sample is discussed.

Mumps—United States, 1980-1983

Anonymous. MMWR 1983 Oct 28;32(42):545-7.

Authors' abstract: As of October 22 (week 42), 1983, 2,683 mumps cases were reported to CDC, which represents a 41% decrease in mumps activity overall, compared to the same period in 1982, and a record low for reports in this period. Twenty-seven reporting areas show decreased numbers of cases for 1983. In 1980, all states reported some mumps activity; whereas in 1981, one state reported no mumps. To date in 1983, four areas are reported free of mumps, compared to three areas in the same period of 1982.

In 1982, 5270 cases of mumps were reported to CDC, for an incidence rate of 2.3 cases per 100,000 population. This is 7% higher than the 1981 total of 4,941 cases, the lowest reported incidence since mumps became a nationally notifiable disease in 1968. The small increase in 1982 was principally due to increased mumps disease in Ohio, which does not require mumps vaccination for school attendance. Ohio had almost three times as many cases in 1982 (1,775 cases) as in 1981 (687). The number of reported cases in other states decreased 17.8% between 1981 and 1982.

During 1967-1976, the highest reported rate occurred in 5- to 9-year-olds, followed by that in children under 5 years old. Together, these two groups accounted for over 70% of all reported cases. However, over the last 5 years (1978-1982), they accounted for only slightly more than 50% of reported cases. During this period, the risk of infection for 10- to 14-year-olds surpassed that for children under 5 years old. National data for 1982 indicate that the risk of infection for 10- to 14-year-olds was higher than that for any other age group.

Mumps Surveillance in England and Wales, 1962-1981

N.S. Galbraith, S.E. Young, J.J. Pusey, D.L. Crombie and J.P. Sparks. Lancet 1984 Jan 14;1(8368):91-4.

Authors' abstract: A study of routine data on mumps in England and Wales suggests that its epidemiological features are changing from those of an epidemic disease in young adults and older children to a more endemic disease in younger children. Infection now occurs at an earlier age, at which complications are less frequent and symptomless infection may be more common. The incidence of clinical disease may be falling. The high proportion of registered deaths in the middle aged and elderly may be an artifact due to misclassification of causes of death and to misdiagnosis. These changes lessen the need for routine immunization. Indeed with low acceptance rates of measles vaccination of 50% at age 15 months, mumps/measles routine vaccination at the same age is contraindicated because similarly low acceptance rates might lead to an increase in the number of cases of mumps in older children and young adults, at which ages complications are more frequent.

Enzyme-Linked Immunosorbent Assay Compared with Neutralization Tests for Evaluation of Live Mumps Vaccines

H. Sakata, M. Hishiyama and A. Sugiura. J Clin Microbiol 1984 Jan;19(1):21-5.

Authors' abstract: Mumps-specific antibody levels before and after vaccination with live mumps vaccines were determined by enzyme-linked immunosorbent assay (ELISA) and neutralization tests. A correlation was found between neutralization titers and optical density in ELISA. However, postvaccination sera from some vaccinees who failed to seroconvert by neutralization contained significant levels of mumps-specific antibody detectable by ELISA. In some of these serum specimens, the antibody directed to the F polypeptide of mumps virus was predominant. Most sera positive in ELISA neutralized mumps virus upon the addition of fresh guinea pig serum to the virus-serum mixture.

Evaluation in Young Children of the Urabe Am 9 Strain of Live Attenuated Mumps Vaccine in Comparison with the Jeryl Lynn Strain

T. Vesikari, F.E. Andre, E. Simoen, G. Florent, E.L. Ala-Laurila, A. Heikkinen, H. Kuusinen and A. Terho. Acta Paediatr Scand 1983 Jan;72(1):37-40.

Authors' abstract: Urabe Am 9, a new strain of mumps vaccine, originally developed in Japan, was evaluated in children 14 to 20 months of age in a comparative trial with the Jeryl Lynn strain. Both vaccines performed well. The antibody responses were measured using a neutralization test and a hemolysis-in-gel test. The seroconversion rates at six weeks, as detected with either one or both tests, were 55/58 (94.8%) after the Urabe Am 9 and 58/60 (96.7%) after the Jeryl Lynn vaccine. Only mild infrequent adverse reactions were observed. It is concluded that both strains of live attenuated mumps vaccine are immunogenic and well-tolerated in this age group.

The Reactogenicity and Immunogenicity of the Urabe Am 9 Live Mumps Vaccine and Persistence of Vaccine Induced Antibodies in Healthy Young Children

W. Ehrengut, A.M. Georges and F.E. Andre. J Biol Stand 1983;11(2):105-13.

Authors' abstract: The immunogenicity and reactogenicity of the Urabe Am 9 mumps virus vaccine strain were studied after the administration of different doses of the vaccine to 197 children ranging in age from seven and a half months to nine years and without a history of mumps. There was no effect of dose on the response in serum neutralizing antibodies in the range of $10^{2.9}$ to $10^{4.7}$ TCID50/dose. In the 90 subjects without detectable serum neutralization antibodies before vaccination seroconversion was obtained in 94.4% after 42 days. Half of a group of 34 seropositive children who were tested also

showed a fourfold or greater rise in antibodies. Persistence of vaccine-enhanced hemagluttinin-inhibition (EHI) antibodies was satisfactory as only two of 56 vaccinees followed up for between 27 and 32 months had undetectable levels of EHI antibodies and the geometric mean titer of vaccine-induced EHI antibodies had only fallen to about one-third by 32 months after vaccination. Although there was serological evidence of a subclinical re-infection in three subjects, to date none of the vaccinees has had clinical mumps indicating that the vaccine confers protection against disease. The vaccine was well tolerated. Furthermore, the majority of the few 'reactions' reported were probably not vaccine-related. It is concluded that the Urabe Am 9 is an acceptable strain for use in live mumps vaccines.

The Immunizing Effect and Reactogenicity of Two Live Attenuated Mumps Virus Vaccines in Swedish Schoolchildren

B. Christenson, L. Heller and M. Bottiger. J Biol Stand 1983 Oct;11(4):323-31.

Authors' abstract: An evaluation of the seroconversion and booster effects after vaccination with two different mumps vaccines, the Urabe Am 9 strain and the Jeryl Lynn strain, was carried out in schoolchildren. Four hundred and fifty-four schoolchildren aged 11 to 12 years with no previous history of mumps or mumps vaccination were enrolled for the study. The antibody responses were measured by serum neutralization (SN) and hemolysis-in-gel (HIG) tests. Of the 454 subjects, 130 were found to be initially seronegative. Two lots of different strengths of each vaccine were used to evaluate the relationships. The Urabe Am 9 vaccine lots had infectivity titers of 100,000 and 19,000 TCID50 per dose and the Jeryl Lynn vaccine titers of 59,000 and 28,000 TCID50 per dose. Only slight differences in seroconversion rates were seen between the lots. The overall seroconversion rate, measured by SN, was 94% for the Urabe Am 9 vaccine and 91% for the Jeryl Lynn vaccine, whereas the geometric mean titer for virus-neutralizing antibody in seroconverting children was 7.4 with the Urabe Am 9 vaccine and 10.7 with the Jeryl Lynn vaccine. In children who were seropositive prior to vaccination, a marked rise in antibody titer was found 8 weeks after vaccine injection indicating a booster effect. The miscellaneous post-vaccination side-effects were mild and inconsequential.

Efficacy of Mumps Vaccine—Ohio

Anonymous. MMWR 1983 Aug 5;32(30):391-2, 397-8.

From authors' discussion: From February 5 through April 23, 1982, 110 cases of mumps were reported among 357 sixth-, seventh- and eighth-grade students in a middle school in Ashtabula County, Ohio. Because the overall attack rate was 31%, the efficacy of the mumps vaccine was investigated.

The methods used to ascertain cases and determine vaccination status greatly affect estimates of vaccine efficacy (VE). Studies relying solely on school records for case-finding and determination of immunization status may provide misleadingly low estimates of efficacy. In this study, the calculated VE improved (from 37% to 85%) with progressively more rigorous methods of case-finding, application of an uniform case definition, better documentation of vaccine history, and use of a setting with presumed more uniform exposure.

As indicated in this outbreak and in a recent study of benefit-cost analysis of mumps vaccine, the considerable medical and economic costs associated with mumps morbidity can best be averted by including mumps immunization as part of state compulsory school immunization laws. Provisional 1982 mumps-incidence data demonstrate that the incidence of mumps disease in states without a compulsory school mumps immunization law (34.7 per million population) was twice as high as in states that have such a law (17.5 per million population).

Other Herpesvirus Infections

Towne-Vaccine-Induced Prevention of Cytomegalovirus Disease After Renal Transplants

S.A. Plotkin, M.L. Smiley, H.M. Friedman, S.E. Starr, G.R. Fleisher, C. Wlodaver, D.C. Dafoe, A.D. Friedman, R.A. Grossman and C.F. Barker. Lancet 1984 Mar 10;1(8376):528-30.

Authors' abstract: Ninety-one renal transplant candidates were randomized to receive Towne strain cytomegalovirus (CMV) vaccine or placebo at least 8 weeks before transplantation. The vaccine was well tolerated and there was no vaccine virus excretion. Serological and cellular immune responses developed in most vaccinees but were lower in the transplant patients than in healthy volunteers and some of the seronegative patients failed to mount responses. CMV infection occurred in most of the seronegative vaccine-treated or placebo-treated patients who received kidneys from seropositive donors, but the illnesses were less severe in the vaccinees than those in similarly exposed placebo-treated patients. Vaccine-treated patients who received kidneys from seronegative donors did not excrete virus, and therefore the vaccine virus was not reactivated from a putative latent state despite immunosuppression at the time of transplantation.

Pneumococcal Infections

Serogroups and Serotypes of Pneumococci in Montreal: Correlations with Age, Outcome and Indications for Vaccination

F. Lamothe, G. Delage, M. Laverdiere and P. Saint-Antoine. Can Med Assoc J 1984 Mar 15;130(6):737-40.

Authors' abstract: The serogroups or serotypes of 262 pneumococcal isolates obtained from the blood and other body fluids of 260 patients in the Montreal area during a 3-year period were determined. The distribution of the 30 different serogroups detected was generally similar to what has been reported in other Canadian provinces and in the United States. However, the distributions in pediatric patients (less than 18 years old) and adults were significantly different ($p < 0.001$). Serogroup 15 was relatively frequent in the adults. In the pediatric patients, 88% and 91% of the 150 isolates were related to the 14-valent and the new 23-valent vaccines, respectively. In the adults the comparable proportions were 70% and 89% of the 112 isolates. The mortality rate was 6% in the pediatric patients and 41% in the adults. Previous use of pneumococcal vaccine in the pediatric patients would have prevented only one death because most were less than 2 years old or did not have conditions regarded as indications for vaccination. Such underlying diseases were found in 58% of the adults, though. The mortality rate was 26% in the adults who were less than 65 years of age and were without these underlying conditions but rose to 65% in older patients; the difference was statistically significant ($p < 0.02$).

Effect of Underlying Disease and Age on Pneumococcal Serotype Distribution

S.J. Weisholtz, B.J. Hartman and R.B. Roberts. Am J Med 1983 Aug;75(2):199-205.

Authors' abstract: The hospital records of 264 patients with 277 episodes of pneumococcal bacteremia occurring at New York Hospital-Cornell Medical Center over the period 1970 to 1980 were examined to determine whether serotype distribution varied with the underlying disease or age of the patient. The patients were placed into three groups according to their underlying disease. Group A consisted of all patients with significant impairment of their immune system. Group B included those patients with underlying conditions that were not associated with immune deficiency. Group C comprised those patients considered to be normal hosts. Overall, 84 percent of blood isolates were serotypes included in the vaccine. In Group A, only 73 percent of these isolates were vaccine types, compared with 85 percent in Group B and 97 percent in Group C (differences significant at $p < 0.001$). Vaccine serotypes were more common in children than adults (92 versus 81 percent), but in analysis that controlled for underlying disease, the elderly did not differ from younger adults in serotype distribution. The apparent predilection of nonvaccine serotypes to cause bacteremia in immunocompromised patients may be one factor limiting vaccine efficacy in this high-risk population.

Long-Term Persistence of Antibody Following Immunization with Pneumococcal Polysaccharide Vaccine

M.A. Mufson, H.E. Krause and G. Schiffman. Proc Soc Exp Biol Med 1983 Jun;173(2):270-5.

Authors' abstract: Thirty-seven healthy volunteers who received a pneumococcal polysaccharide vaccine were tested 4, 5, or 6 years after immunization for circulating type-specific pneumococcal antibody by radioimmunoassay of their sera. Each volunteer was immunized with one of four different pneumococcal vaccines containing 50 micrograms of each of 6, 8, 9, or 13 capsular polysaccharides; a few volunteers received octavalent or tridecavalent pneumococcal vaccines combined with bivalent influenza virus vaccine in a single syringe. Four years after immunization, the mean antibody level was 90% of the level achieved 4 weeks after vaccination. Among volunteers tested 5 years after immunization (including three 6 years after vaccination), the mean antibody level was 76% of that 4 weeks after inoculation. These findings confirm the long-term persistence of vaccine-induced type-specific pneumococcal antibodies and suggest that the interval between repeated doses of pneumococcal vaccine should be at least 5 years.

Antibody Responses After Immunization with Polyvalent Pneumococcal Vaccine Containing 10, 25, or 50 Micrograms of 14 Polysaccharide Types Per Dose

F.R. Cano, M.V. Querry, C.J. Tarrant, M.B. Ritchey and G. Schiffman. Proc Soc Exp Biol Med 1983 Sep;173(4):579-82.

Authors' abstract: Immune responses were determined to three different doses of a pneumococcal vaccine which contained 10, 25, or 50 micrograms of 14 polysaccharide types (1, 3, 4, 6A, 6B, 7F, 8, 9N, 12F, 14, 18C, 19F, 20, and 23F) per dose. Pre- and 4-weeks postvaccination sera were examined by radioimmunoassay. Ratios of geometric mean titers (GMT) showed a greater than threefold increase of antibodies to each type of polysaccharide regardless of the dose of antigen. The post-GMT was highest to 12 of 14 types in recipients of the 25-micrograms vaccine. Subjects in the group receiving a 25-micrograms dose of each antigen showed more two- and fourfold titer increases than did subjects in the group receiving 10- and 50-micrograms doses, but, in general, seroconversion rates were similar in all the groups. All GMT values in the 25-micrograms vaccine group were well above what is currently considered to be the protec-

tive level of antibody. Local reactions, overall, were low in all groups. Pain, induration, and tenderness at the site of injection, which were greatest in recipients of the 50-micrograins dose/antigen, were progressively lower with the 25- and 10-micrograms dose/antigen.

Antibody Response to Pneumococcal Vaccination in Children Younger Than Five Years of Age

R.M. Douglas, J.C. Paton, S.J. Duncan and D.J. Hansman. J Infect Dis 1983 Jul;148(1):131-7.

Authors' abstract: Sera were analyzed by radioimmunoassay for type-specific pneumococcal antibody in 249 children aged six to 54 months, who were participating in a controlled trial of a 14-valent pneumococcal vaccine. Levels of serum antibody to all serotypes increased after immunization in all age groups tested. For all serotypes, the antibody response increased progressively with age whether response was viewed as antibody doubling, relative increare in geometric mean, or final antibody level. Responses were poor up to the age of five years for the important pediatric serotypes 6A, 14, 19F, and 23F. Seventeen children under the age of two years at the time of primary immunization received booster doses of vaccine six months later. There was no significant increase in antibody to any serotype, and the geometric mean antibody levels fell for most types. Immune response to the pediatric serotypes was poor until the age of 4.5 years.

Pneumococcal Vaccine in Normal Children. Primary and Secondary Vaccination

E.M. Lawrence, K.M. Edwards, G. Schiffman, J.M. Thompson, W.K. Vaughn and P.F. Wright. Am J Dis Child 1983 Sep;137(9):846-50.

Authors' abstract: A pneumococcal polysaccha ide vaccine containing 50 micrograms of each of 14 pneumococcal types was administered to 79 children 2 to 5 years of age. In earlier studies, 52 of these children had received pneumococcal vaccine; 27 had received a placebo. Local reactions were significantly greater in the reimmunized group. Antibody response to the vaccine was similar in both groups. Mean fold rises to most vaccine components were at least twofold. The response to specific pneumococcal types was unrelated to the frequency with which each type causes illness. Response to type 6 continued to be poor for children up to age 5 years. A vaccine with improved immunogenicity must be developed before widespread use in normal children is advocated. However, the 14-valent pneumococcal polysaccharide vaccine currently available is moderately immunogenic in children by age 2 years and should be given to patients with increased risk of pneumococcal illness at that time.

Pneumococcal Vaccine in the Hospital. Improved Use and Implications for High-Risk Patients

R.S. Klein and N. Adachi. Arch Intern Med 1983 Oct;143(10):1878-81.

Authors' abstract: A randomized trial of a program to improve pneumococcal immunization was undertaken. Also studied were the prevalence of high-risk conditions for serious pneumococcal disease among hospital admissions and prior hospitalization of patients with pneumococcal bacteremia. During two successive winters, 56% of 1,062 medical patients were identified by admission diagnosis or age as having a high-risk condition. None had received prior vaccination. During the trial period, identifying candidates for vaccination increased immunization from two (2.1%) of 95 to ten (10.4%) of 96 in year 1 and from two (2.1%) of 96 to 19 (20%) of 95 in year 2. Among adults with pneumococcal bacteremia, 33 (54%) of 61, including 32 (64%) of 50 with high-risk conditions, had documentation of prior hospitalization within five years. A hospital-based program can increase pneumococcal immunization rates and would be directed at patients in whom serious pneumococcal disease is likely to develop.

Antibody Response to Pneumococcal Vaccine in Patients with Solid Tumors and Lymphomas

R.A. Shildt, J.F. Boyd, J.D. McCracken, G. Schiffman and J.P. Giolma. Med Pediatr Oncol 1983;11(5):305-9.

Authors' abstract: Ninety patients with solid tumors or lymphomas were immunized with a polyvalent pneumococcal vaccine. Pre- and postimmunization antibody titers were determined by radioimmunoassay. Treated patients with lymphoma had poor antibody response whether on or off chemotherapy. Patient with chronic lymphocytic leukemia had the lowest antibody titers of all patients groups. Patients with solid tumors had antibody responses which were similar to those of the control population. Those patients who received sequential chemotherapy and immunization had a tendency for higher postimmunization titers than those patients who received simultaneous chemotherapy and immunization, but the difference was not significant. This study suggests that patients with solid tumors would be expected to benefit from pneumococcal immunization, whereas patients with lymphoma immunized after receiving treatment initially would not be expected to develop protective antibody levels. Recovery of antibody formation in patients with non-Hodgkin lymphoma, which may occur in patients with Hodgkin disease, remains to be determined.

Pneumococcal Vaccine and Otitis Media in Infancy

P.H. Makela, P. Karma and M.K. Leinonen. Bull Eur Physiopathol Respir 1983 Mar-Apr;19(2):235-8.

Authors' abstract: This is a review of present knowledge about the chances of preventing otitis media (OM) by vaccination. Studies of experimental pneumococcal OM in the chinchilla, and observations on serum antipneumococcal antibody levels in children in connection with OM morbidity suggested that protective immunity could be achieved by vaccination. On the other hand, many of the pneumococcal polysaccharides—including those four types that are most common in OM—are not highly immunogenic in infants younger than 2 years. The highest incidence of OM coincides with that very age of low responsiveness. Four large field studies in USA and Finland have shown that vaccination with 14-valent pneumococcal vaccine does prevent recurrent as well as first-time OM caused by species to which good immune response is obtained. Because the most common pneumococci do not belong to this category, the overall protective effect of such vaccination remains low (10 to 15% in the studies reported). Thus the present vaccine cannot be recommended for prevention of OM in infants younger than 2 years. The data strongly encourages efforts in vaccine development, in ways that improve immunogenicity in infants.

Use of Pneumococcal Polysaccharide Vaccine in Preventing Otitis Media in Infants: Different Results Between Racial Groups

V.M. Howie, J. Ploussard, J.L. Sloyer and J.C. Hill. Pediatrics 1984 Jan;73(1):79-81.

Authors' abstract: A total of 133 children between 6 and 11 months of age with at least one episode of otitis media were given one of two pneumococcal vaccines. One vaccine contained 25 microns of types 1, 3, 6, 7, 14, 18, 19, and 23 and the other vaccine (control) contained 25 microns of types 2, 4, 5, 8, 9, 12, and 25. Follow-up care of the 65 black infants revealed significantly more otitis media visits in those infants receiving the control vaccine. Among the 68 white infants there was no difference between control and vaccine groups after vaccination.

Antibody Response to Pneumococcal Vaccine in Splenectomized Children

F.K. Pedersen. Acta Pathol Microbiol Immunol Scand [C] 1983 Apr;91(2):169-80.

Author's abstract: The antibody response, measured as total immunoglobulin, of 66 splenectomized children to a 14-valent pneumococcal capsular polysaccharide vaccine was determined by an enzyme-linked immunosorbent assay. It did not differ significantly from that of 12 non-splenectomized children for 10 of the 14 polysaccharide antigens studied, but was lower for polysaccharide types 2, 3, 8 and 12F. Significant responses of both IgG and IgM antibody against all four antigens studied were found in 10 splenectomized and against all 14 antigens in five non-splenectomized children. In 2/10 splenectomized and 1/5 non-splenectomized children the arbitrary IgG/IgM ratio was below 1 in contrast to the pattern found in the other 12 patients. The increase in antipneumococcal antibody after vaccination in seven non-splenectomized children receiving corticosteroid therapy was only significantly lower than that of 12 untreated non-splenectomized children against two of the 14 antigens, and similar or higher against all antigens in five splenectomized children receiving steroid therapy compared to 66 splenectomized children not receiving such therapy. In 22 splenectomized children 70% of the peak geometric mean total antibody concentration four weeks after vaccination was still present after two years. Adverse reactions to the vaccine included local reactions at the vaccination site in 56% and fever in 9%. Side-effects were correlated to the geometric mean concentration of total antibody present at the time of vaccination. Immunogenicity of each of the 14 vaccine antigens varied considerably, as did the responses of different individuals.

Immunoglobulin Classes and Persistence of Anti-Pneumococcal Antibodies in Splenectomized Adults and Adolescents After Pneumococcal Vaccination

F.K. Pedersen, J.L. Nielsen and J. Ellegaard. Acta Pathol Microbiol Immunol Scand [C] 1983 Aug;91(4):245-9.

Authors' abstract: The IgG-, IgM- and IgA- antipneumococcal antibody response to pneumococcal vaccination in 29 splenectomized adults and adolescents with hereditary spherocytosis or previous traumatic splenic rupture was determined by an enzyme-linked immunosorbent assay. It was not significantly different from that of 12 healthy controls except for a lower IgM class antibody increase in the splenectomized against one of four antigens studied. The antibody response was predominantly of IgG class, but significant increases in IgM and IgA class antibodies against all four antigens (polysaccharide types 2, 6A, 12F and 14) studied were observed. In 1/29 splenectomized and 2/12 healthy individuals (7%) the IgG antibody class did not predominate. In 36 adults and adolescents splenectomized due to traumatic rupture or during surgery for gastric ulcer, 77% of the peak geometric mean total antibody concentration four weeks after vaccination was still present after 21 months (16-26 months).

Response of Traumatized Splenectomized Patients to Immediate Vaccination with Polyvalent Pneumococcal Vaccine

E.S. Caplan, H. Boltansky, M.J. Snyder, J. Rooney, N.J. Hoyt, G. Schiffman and R.A. Cowley. J Trauma 1983 Sep;23(9):801-5.

Authors' abstract: In recent years the syndrome of overwhelming post-splenectomy sepsis has been increasingly reported in adults. Since more than 50% of these infections are caused by pneumococcus these post-splenectomy patients are considered a suitable group to receive the pneumococcal vaccine. Previous studies of the response obtained in post-splenectomy patients have been conflicting and we found no study that looked at the response to immediate vaccination in this group of patients. Sixteen consecutive multitraumatized patients received polyvalent pneumococcal vaccine 0.5 ml IM within 72 hours of splenectomy and 10 normal controls were given 0.5 cc polyvalent pneumococcal vaccine. Patients received an average of 19.2 units of blood and blood products; seven were on steroids for concomitant head injury. Antibody was measured by the radioimmune assay. Most of the subjects of both groups responded to at least seven of the 12 measured antigens and no patient in the control group and only one in the splenectomized group responded to all 12 antigens. When rate of response to individual serotypes was compared no difference was found between the two groups. Comparison of geometric mean fold rise and fold rise between the two groups for each of the 12 serotypes revealed essentially no difference. We conclude the response to polyvalent pneumococcal vaccine among polytrauma splenectomized patients is similar to that of normal controls, and that the vaccine can be administered immediately post-splenectomy.

Reactions to Booster Pneumococcal Vaccination in Patients with Sickle Cell Disease

J.G. Rigau-Perez, G.D. Overturf, L.S. Chan, J. Weiss and D. Powars. Pediatr Infect Dis 1983 May-Jun;2(3): 199-202.

Authors' abstract: Repeat (booster) pneumococcal vaccination was administered to 32 patients with sickle cell disease in a double blind, placebo-controlled crossover study as early as 2.3 years after initial immunization. A significantly greater proportion of patients reported local pain, swelling or redness after booster, as compared to that after placebo ($p < 0.001$), and pneumococcal antibody titer before vaccination was the predominant predictive variable for the development of fever, local pain and swelling after booster. A comparison of reaction rates following primary or booster immunization showed no significant differences in the frequency of reported symptoms except for muscle pain which occurred less frequently after booster ($p < 0.005$). The concern for adverse reactions after repeat pneumococcal vaccination should not be an obstacle to the pursuit of further studies on the efficacy of pneumococcal vaccine and booster responses.

B-Cell Immunodeficiency in Acquired Immune Deficiency Syndrome

A.J. Ammann, G. Schiffman, D. Abrams, P. Volberding, J. Ziegler and M. Conant. JAMA 1984 Mar 16;251(11): 1447-9.

Authors' abstract: To investigate B-cell function in acquired immune deficiency syndrome (AIDS), we immunized a group of patients with AIDS with pneumococcal polysaccharide (tetradecavalent) and protein (keyhole-limpet hemocyanin) antigens. Antibody responses were determined three to four weeks after immunization. Compared with controls, patients with AIDS had significantly lower geometric mean antibody levels to polysaccharide before and after immunization. Levels before and after immunization were frequently below a level thought to correlate with protection. Patients with AIDS also had a significant reduction in their primary antibody response to the protein antigens. The results of these studies indicate that AIDS is associated with an acquired B-cell as well as T-cell immunodeficiency. It is suggested that future studies should consider the evaluation of passive antibody in the prevention of infection and/or prevention of progressive immunodeficiency.

Poliomyelitis

Technics and Strategy in the Treatment of Severe Paralytic Scoliosis (French)

J.G. Pous, A. Dimeglio, J. Adrey and Y. Jarrousse. Rev Chir Orthop 1983;69(5):393-406.

English summary: Sixty-three paralytic scolioses with severe disability have been treated between 1973 and 1982. Fifty-two were due to poliomyelitis. The average angular deformity was 95.8 degrees and was related to delay in treatment and rapid progress of the curve. All cases were operated on. Spine fusion was performed either by the anterior approach (Dwyer or V.D.S.) or by a posterior approach (Harrington or Harrington-Luque). The pre-operative management was based on Cotrel or Halo traction. There were several complications—three non-unions, three neurological impairments, and nine cases of sepsis. It was concluded that the pre-operative management should be as short as possible, that the spine fusions should be done systematically and that any paralytic scoliosis increasing by more than 10 degrees a year between the ages of 8 and 10 years should be operated on early. This type of treatment should lower the incidence of severe disability and allow good functional and educational rehabilitation. The degree of diminished growth of the spine was moderate.

Adult Polio-Like Syndrome Following Enterovirus 70 Conjunctivitis (Natural History of the Disease)

B.C. Katiyar, S. Misra, R.B. Singh, A.K. Singh, S. Gupta, A.K. Gulati, S. Christopher and T.J. John. Acta Neurol Scand 1983 May;67(5):263-74.

Autnors' abstract: During the Indian EV 70 conjunctivitis epidemic in 1981, 79 patients with neurological complications were evaluated by clinical, electrophysiological, histopathological and virological studies. The disease was heralded by an attack of conjunctivitis and was followed, after a variable latent period, by a preparalytic, paralytic, and post-paralytic stage of slow recovery. The above events occurred in an orderly sequence. The paralysis affected the cranial nerves, limbs or both. The clinical course closely simulated poliomyelitis, without any evidence of radiculopathy or myelopathy. Cranial nerve palsies were seen in approximately half of the patients. The electrophysiological and histological studies pointed towards the affection of anterior horn cells. The raised neutralizing antibody titers to enterovirus 70, confirmed the etiology of the disease. On the available data, we believe that this nosological entity should be considered under the general title of "polio-like syndrome" following EV 70 conjunctivitis. On account of two epidemics in 1971 and 1981 with unfavorable prognosis and high resultant disability, and because of lack of specific therapy, it has become imperative to develop, as a top priority, a vaccine for immunization.

Late Post-Poliomyelitis Muscular Atrophies. Report of Fourteen Cases (French)

G. Serratrice and L. Milandre. Sem Hop Paris 1984 Jan 26;60(3):149-53.

English summary. The authors report 14 cases of late post-poliomyelitis muscular atrophies. The atrophy appears many years after the acute episode of anterior poliomyelitis. Several types of disorders were observed: extension of weakness and wasting; chronic spinal amyotrophy; amyotrophic lateral sclerosis without bulbar atrophy; coincidental muscular dystrophy. These cases have been interpreted in different ways. Further studies are necessary.

Differential Resistance to Paralytic Poliomyelitis Controlled by Histocompatibility Leukocyte Antigens

W. van Eden, G.G. Persijn, H. Bijkerk, R.R. de Vries, R.K. Schuurman and J.J. van Rood. J Infect Dis 1983 Mar;147(3):422-6.

Authors' abstract: To investigate whether genetic factors encoded by the histocompatibility leukocyte antigen (HLA) complex influence resistance to poliomyelitis, the pattern of inheritance of HLA haplotypes within affected families was studied. Seventeen informative families were available from a genetically homogeneous, unvaccinated community in The Netherlands after a single epidemic of poliomyelitis. Whereas none of 17 other polymorphic markers deviated from the expected Mendelian pattern of inheritance, the inheritance pattern of HLA haplotypes did. In sibpairs consisting of a patient with paralytic poliomyelitis and a nonparalytic control sib, significantly less sharing of HLA haplotypes was observed than would be expected by chance alone ($p=0.014$). The sharing of HLA haplotypes between patients with nonparalytic poliomyelitis and healthy controls did not deviate significantly from the expected value. These data suggest that HLA-encoded genetic factors control resistance to the paralytic form of poliomyelitis.

Patterns of the Epidemic Process in Poliomyelitis with Regular Live Vaccine Immunization of the Population (Russian)

V.I. Votiakov and E.V. Feldman. Zh Mikrobiol Epidemiol Immunobiol 1983 Jan;(1):74-8.

English summary: The results of the study of epidemic poliomyelitis in Byelorussia in 1978-1981 are presented. Two consecutive phases of the epidemic process were established: the suppression of the infection and its elimination. In the suppression phase sporadic cases of poliomyelitis still persisted, due to reduced circulation of wild polioviruses. In the elimination phase no wild polioviruses were isolated and no cases of the disease occurred.

Prevalence, Incidence, and Epidemiological Features of Poliomyelitis in the Yemen Arab Republic

M.M. Hajar, A.S. Zeid, M.A. Saif, M.A. Parvez, R.C. Steinglass and S. Crain. Bull WHO 1981;61(2):353-9.

Authors' abstract: There is a lack of reliable information on the extent of the poliomyelitis problem in developing countries, although the disease is thought to be more of a threat in urban than in rural areas. The Expanded Program on Immunization (EPI) began operations in Yemen in 1977, and it was considered appropriate to try to establish the prevalence of residual paralysis due to poliomyelitis in children aged 5-13 years, in order to estimate the annual incidence of clinical cases of the disease, and to determine the epidemiological features of poliomyelitis in the country. The data thus obtained would provide a basis for assessing the impact of the immunization program on the incidence of poliomyelitis.

The results of the survey showed a prevalence of lameness due to poliomyelitis of 4.0 per 1000 children. The estimated annual incidence of the disease is thus 18.6 per 100,000 of the general population, or approximately 1088 cases each year, with an estimated 163 deaths. An estimated 5000 children aged 5-13 are lame as a result of poliomyelitis. There was no significant difference in the incidence of the disease in rural and urban areas. The median age of onset was 1.92 years in the urban setting

and 1.29 years in the rural setting, with more than half of all cases occurring before the age of 2 years. Although a national disease notification system was established in 1976, 95% of the clinical cases discovered during the survey had not been reported. This underlines the importance of special surveys in gathering the data necessary to evaluate the effectiveness of the immunization program.

Estimation of Incidence of Poliomyelitis by Three Survey Methods in Different Regions of the United Republic of Cameroon

D.L. Heymann, V.D. Floyd, M. Lichnevski, G.K. Maben and F. Mvongo. Bull WHO 1983;61(3):501-7.

Authors' abstract: Surveys were conducted in one urban and two rural regions of the United Republic of Cameroon to estimate the annual incidence of paralytic poliomyelitis. Three different survey methods were used: a review of hospital and clinic registers, a school survey, and a house-to-house survey. The house-to-house survey identified the highest number of lame children and gave estimates of incidence of between 18.8 and 32.6 per 100,000 population in the three regions. The estimates of incidence obtained by the two other survey methods in the urban region did not differ significantly from that obtained by house-to-house survey, but in the rural regions, were significantly lower. It is concluded that house-to-house surveys are a sensitive method of identifying lame children in both urban and rural regions. School surveys and review of hospital and clinic registers, while equally sensitive in urban regions, are less sensitive in rural regions and may significantly underestimate the annual incidence of paralytic poliomyelitis. These limitations should be borne in mind when using the survey methods.

Killed Polio Virus Vaccine in the Control of Poliomyelitis in Finland

K. Lapinleimu. Ann Clin Res 1982;14:199-203.

Author's abstract: In the prevaccination era in Finland paralytic polio cases were reported every year. The incidence in the last two epidemic years, 1954 and 1956, was about 14/100,000 inhabitants per year. Mass vaccination was carried out in 1960-1961. Finland has relied solely on the killed polio vaccine (KPV). The last patients with indigenous polio were found in 1961 and there were two imported cases in 1964. Infants have been vaccinated systematically at Child Health Centers over a period of 20 years. In the preschool age group the vaccination rate is close to 98%.

Despite the absence of cases of poliomyelitis, an intensive search for polio viruses was carried out in 1972-1974. It was directed at patients with polio-like diseases, at preschool children and at sewage. Enteroviruses were isolated from 30% of the patients with polio-like diseases without a single isolation of polio viruses. Before mass vaccination, polio viruses were isolated from 28% of such patients. Among 4878 preschool children examined, 16% excreted viruses in feces, but none were polio. Examination of sewage gave virus isolations (mostly Coxsackie B viruses) in 65% without a single polio isolation. These data indicate that KPV had eliminated not only polio disease but also polio virus from Finland. The elimination of polio viruses has not been followed by an upsurge of other enteroviruses producing polio-like diseases.

Studies on immunity showed that an unexpectedly high proportion of our preschool children lacked antibodies to type 1 and especially to type 3. In response to a booster dose, however, the children gave a secondary-type reaction indicating immunity. Although antibody levels were low and even undetectable in some, immunity has been sufficient to protect us against imported polio viruses. The maintenance of immunity in the population requires the vaccination of all infants. Instead of the KPV used routinely at present, we are expecting in the near future the newly developed more potent KPV, which induces long-lasting immunity with fewer injections.

Results of a Program Successfully Combining Live and Killed Polio Vaccines

E.E. Lasch, Y. Abed, C.B. Gerichter, M.E. Massri, O. Marcus, R. Hensher and N. Goldblum. Isr J Med Sci 1983 Nov;19(11):1021-3.

Authors' abstract: Oral polio vaccine (OPV) has been used in the Gaza Strip since 1968. Although vaccine coverage had reached 80 to 90% of the infant population, the epidemiological pattern of the paralytic disease had not changed significantly as of the beginning of this study. The mean annual incidence continued to be around 10/100,000. Two outbreaks occurred, in 1974 and 1976, involving 75 and 77 children, respectively, an incidence of 18/100,000. In these two outbreaks, 34 and 50% of the affected children, respectively, received 3 to 4 doses of OPV. A serological survey done after a vaccination campaign with monovalent Type 1 vaccine showed an unexpectedly low percentage of seropositives. A parallel was found between the prevalence of diarrheal disease and vaccine failure, and a causal effect was postulated. To overcome this problem, a program of immunization was started early in 1978 combining both live and killed polio vaccines. Although cases of polio continue to appear, the incidence has been reduced to 2.4/100,000 population. In 1981, only one case was reported, in an unvaccinated child. Thus, it would seem that the new vaccination schedule combining live and killed vaccines makes eradication of polio a possibility.

Antigen Content of Inactivated Poliovirus Vaccine for Use in a One- or Two-Dose Regimen

J. Salk, P. Stoeckel, A.L. van Wezel, K. Lapinleimu and G. van Steenis. Ann Clin Res 1982 Dec;14(5-6):204-12.

Authors' abstract: The immunologic response to inactivated poliovirus vaccine following one and two doses has been studied in infants in developing and developed countries using vaccine prepared at the Rijks Instituut voor de Volksgezondheit, The Netherlands. Virus was grown in microcarrier cultures of monkey kidney cells, purified, concentrated, and inactivated with formalin. The vaccines used contained different quantities of D-antigen units for each of the three types. The data reveal that both antibody and immunologic memory (booster-type responsiveness) were induced in virtually all individuals following a single dose of a sufficient quantity of antigen. Immunologic memory was readily revealed by the booster-type response following a second dose given six months after the first. The degree of booster-type response to a second dose is linked primarily to the quantity of antigen used for primary immunization, and secondarily to the quantity of antigen used for the booster dose. The data base is presented for formulating the antigen content of an inactivated poliovirus vaccine that can be relied upon to be protective after the first dose when given alone or when incorporated with combinations of other antigens (diphtheria-pertussis-tetanus) that may require two or more doses.

The Trend of Acquired Immunity with Live Poliovirus Vaccine and the Effect of Revaccination: Follow-Up of Vaccinees for Ten Years

O. Nishio, Y. Ishihara, K. Sakae, Y. Nonomura, A. Kuno, S. Yasukawa, H. Inoue, K. Miyamura and R. Kono. J Biol Stand 1984 Jan;12(1):1-10.

Authors' abstract: The persistence of neutralizing antibody (NA) against three types of poliovirus acquired after two doses of trivalent live attenuated poliovirus vaccine (LPV) has been followed up for ten years in individual vaccinees. Sixty-seven children were bled once a year over a five-year period following the primary vaccination. More than 80% of them retained NA against all three types of poliovirus. Thirty-two individuals whose NA titers were 1:16 or over for types 1 and 2 and 1:4 or over for type 3 at the fifth year were further followed up for a further five years and it was shown that during this period some of them had a naturally-acquired antibody rise, mostly against type 3 virus. At the sixth to eighth year after the primary vaccination, one further dose of the trivalent vaccine was administered to the children whose NA titers were down to 1:8 or less and the effect of booster vaccination on NA was followed. Other subjects were revaccinated with LPV and their fecal excretion of the vaccine virus was investigated. The results showed that a decrease in serum antibody level could be a good indicator of the local resistance of the alimentary tract and that reinfection could occur if serum NA had decreased to 1:8 or less, which allowed a virus excretion in the stools.

Antibody Response to Oral Polio Vaccine in Premature Infants

P. Smolen, R. Bland, E. Heiligenstein, M.R. Lawless, R. Dillard, and J. Abramson. J Pediatr 1983 Dec;103(6): 917-9.

From authors' conclusion: Whatever the theoretical considerations, our data indicate that a preterm infant's response to OPV is not influenced by the child's degree of prematurity, birth weight, severity of neonatal problems, sepsis, hyperbilirubinemia, blood transfusions, or concomitant administration of DTP. These data indicate that preterm infants can be effectively immunized with OPV beginning at 2 months of chronologic age, and support the recommendation to begin immunization of premature infants at that time, as long as the child has left the hospital and is not ill.

Problems of Live Virus Vaccine-Associated Poliomyelitis: A Paralytic Case with Isolation of All Three Poliovirus Types

T. Mertens, W. Schurmann, J. Kruppenbacher, K. Rheingans, K. Kellermann, G. Maass and H.J. Eggers. Med Microbiol Immunol (Berl) 1983;172(1):13-21.

Authors' abstract: The case of a 4-month-old girl is described who developed a paralytic polio-like syndrome 3 weeks after oral polio vaccination (OPV). All three poliovirus types could be isolated (9 days after onset of disease polio type 2, and 33 days after onset of disease types 1 and 3, respectively). In order to classify these isolates as Sabin (vaccine)-like (SL) or non-Sabin-like (non-SL), several markers were tested in three laboratories [intratypic serodifferentiation, reproductive capacity at supraoptimal temperature (RTC), $Al(OH)_3$ gel elution assay, and oligonucleotide mapping]. The results of the marker determinations were not uniform, but—summarizing all data—it seems plausible to associate the disease with the OPV. The significance of marker determinations in proving a vaccine-induced poliomyelitis is discussed in the light of this clinical case. Some comments are made on poliovirus vaccination policy in developed countries.

Unusual Complications of Poliomyelitis Vaccination (German)

H.J. Dietzsch and W. Kiehl. Kinderarztl Prax 1983 Nov;51(110):513-6.

English summary: Among 1.5 million children vaccinated with oral polio vaccine between 1969 and 1982 in the County of Dresden, we observed 3 cases suffering

from symptoms which obviously occurred in connection with the vaccination and may possibly have been caused by it. The recurring convulsions, pathological findings in the spinal fluid and electroencephalograms led us to classify these cases as encephalopathies. Onset of symptoms began 4 to 14 days after the administration of monovalent vaccine, type II and monovalent vaccine, type III, respectively, in two of the children and the administration of trivalent vaccine in the third.

Authors go on to review the literature about convulsion reactions after one poliomyelitis vaccination and discuss the pathogens and contraindications fixed by law. Recommendations for comprehensive diagnostic measures for such cases are also given.

Rabies

Nosocomial Rabies: Investigation of Contacts of Human Rabies Cases Associated with a Corneal Transplant

L.J. Anderson, L.P. Williams, Jr., J.B. Layde, F.R. Dixon and W.G. Winkler. Am J Public Health 1984 Apr;74(4):370-2.

Authors' abstract: In October 1978 in Boise, Idaho, a woman died of rabies after receiving a corneal transplant from a man, who in retrospect was also found to have died of rabies. Investigation of 203 contacts of these two patients identified 94 who were felt to have had sufficient risk of exposure to justify being given rabies post-exposure prophylaxis. Nurses, physicians, respiratory therapists, and family members were at greatest risk. We discuss the problems encountered in determining risk of exposure for contacts of humans with rabies.

The Epidemiology of Human Rabies Postexposure Prophylaxis, 1980-1981

C.G. Helmick. JAMA 1983 Oct 21;250(15):1990-6.

Author's abstract: Little is known about the epidemiology of human rabies postexposure prophylaxis (PEP), an important problem whether examined by the cost, the number of persons treated, or the public health resources required. Twenty-one states participated in a surveillance of PEP in 1980-1981. When state health departments were involved, PEP was given correctly to at least 88% of persons. The highest incidence of PEP was in young people up to age 15 years, males, and those in rural areas. Postexposure prophylaxis occurred primarily during the spring, summer, and fall months. The epidemiology of PEP varies depending on the source of exposure and age. Domestic animals and rodents-lagomorphs accounted for PEP far out of proportion to their small role in animal rabies. Postexposure prophylaxis can be prevented for many by not keeping wild animals as pets and reduced by having physicians consult with state or local health departments before starting treatment.

Pre-Exposure Prophylaxis in Peace Corps Volunteers with Intradermal Human Diploid Cell Rabies Vaccine

F.W. Rosa. J Trop Med Hyg 1983 Apr;86(2):81-4.

Author's abstract: The Peace Corps has had approximately 60,000 person/years of experience with rabies pre-exposure duck embryo vaccine (DEV) immunizations, which are required in 80% of volunteer assignments. Rabies exposure treatment rate is much higher in these areas than in the United States. One death from rabies has occurred despite pre-exposure injections. One death also occurred from serum hepatitis contracted in local emergency management of an anaphylactic reaction to duck embryo vaccine. A query to the Peace Corps field medical offices obtained reports of 21 serious reactions in approximately 8,000 duck embryo immunizations. Two thirds of the reactions occurred with the first injection. Only a third of titers measured after four injections of DEV achieved a protective level of greater than or equal to 1:16. Because of these problems human diploid intracellular vaccine (HDCV) was studied in areas where it was available. Because of the high cost and initial short supply, intradermal injections of 0.1 ml HDCV were given. 567 of 570 persons achieved adequate titers. No systemic reactions were reported with intradermal HDCV.

Smallpox and Vaccinia

Five Years of Freedom from Smallpox

I.D. Ladnyi, Z. Jezek and A. Gromyko. J Hyg Epidemiol Microbiol Immunol 1983;27(1):1-12.

Authors' abstract: In 1967, when the intensified global eradication program was launched, smallpox was still endemic in 35 countries with a total population of 1200 million and caused an estimated 10-15 million cases, resulting in 2 million deaths. Ten years and ten months later, on 26 October 1977 through intensified public health activities, the chain of smallpox transmission was finally broken in Merka, south Somalia; the World Health Organization missed its ten-year target line by ten months. In December 1979, the Global Commission concluded that the global eradication of smallpox had been achieved and the Organization formulated its policy for the post-eradication era. In May 1980, the 33rd World Health Assembly endorsed the Commission's conclusion and officially confirmed the international acceptance of smallpox eradication as the most outstanding achievement in international public health. This achievement has unmistakably demonstrated that the concept of dis-

ease eradication is correct and feasible. WHO encouraged countries to discontinue smallpox vaccination and/or the need for a smallpox vaccination certificate from international travellers. However, WHO is continuing its vigilance over the disease and promoting further research on orthopoxviruses. Globally, US$ 313 million were spent on the eradication of smallpox from the world. However, conservative calculations indicate that in the post-eradication era, concrete economic returns resulting from the eradication of smallpox throughout the world, are estimated at US$ 1,000 to 2,000 million, annually. For the last five years of smallpox-free status, savings of about US$ 5,000-10,000 million could be diverted for other health projects, which has had a major impact on international public health. However, there are other dividends similarly worthy as those of economic value. The most important of these are the hundreds of thousands of experienced and dedicated health workers who remain now in the countries as a solid base for implementing other important public health programs.

Subacute Sclerosing Panencephalitis

Persistent Measles Infection of the Central Nervous System: Subacute Sclerosing Panencephalitis

J.L. Sever. Rev Infect Dis 1983 May-Jun;5(3):467-73.

Author's abstract: Measles can persist in the central nervous system and cause subacute sclerosing panencephalitis (SSPE), a progressive disease that is almost always fatal. The ciinical findings of SSPE include behavioral changes, ataxia, seizures, and mental-motor deterioration that begins several years after natural infection with the virus. Measles antibody is found in the spinal fluid, and its presence is particularly useful in establishing the diagnosis. The mechanisms of pathogenesis of SSPE apparently involves the selection of clones of virus, which do not replicate to become complete virus particles. These "suppressed" viruses are able to multiply and spread from cell to cell. The immune system of the patient is unable to clear this infection. Several hypotheses are advanced to expiain these events. Further studies are needed, however, to develop a complete understanding of the pathogenesis of these diseases. Fortunately, SSPE is disappearing in the United States. This apparently is related to the widespread use of measles vaccines and to the resulting low frequency of natural measles infections.

Defective Translation of Measles Virus Matrix Protein in a Subacute Sclerosing Panencephalitis Cell Line

M.J. Carter, M.M. Willcocks and V. ter Meulen. Nature 1983 Sep 8-14;305(5930):153-5.

Authors' abstract: Subacute sclerosing panencephalitis (SSPE) is a slowly progressing fatal human disease of the central nervous system (CNS) that is associated with measles virus persistence. Virus nucleocapsids are present in the brain and the patient is in a state of hyperimmunization towards this agent. However, although all other structural polypeptides are recognized by the immune system, there is a markedly decreased antibody response towards virus matrix or membrane protein. Matrix protein has not been detected in brain cells and infectious virus is not present. The absence of this virus structural polypeptide is thought to account for the apparent restriction in virus maturation both in vivo and in vitro. SSPE viruses can only rarely be rescued from brain tissue by co-cultivation or cell fusion techniques using tissue culture cell lines susceptible to measles virus infection. Often this procedure fails to yield a lytic budding virus but produces instead a carrier cell line in which the agent is cell associated. These lines (known as SSPE cell lines) also do not contain matrix protein. However, the reason for this deficiency is unknown. We have therefore now examined an SSPE cell line which does not yield infectious virus in order to define this process further. We found that although messenger RNA for membrane protein was present, it was unable to form normal matrix protein in translation reactions.

Subacute Sclerosing Panencephalitis: An Immune Complex Disease?

A. Sotrel, S. Rosen, M. Ronthal and D.B. Ross. Neurology (NY) 1983 Jul;33(7):885-90.

Authors' abstract: Vascular osmiophilic deposits of entangled tubular profiles were demonstrated by electron-microscopy in the cerebral tissue of a patient with subacute sclerosing panencephalitis. Measles viral antigen, IgG, IgM, and C3 were found in the same distribution, indicating that the deposits represent immune complexes. To our knowledge, this is the first demonstration of immune complexes in the vessels of the central nervous system.

Subacute Sclerosing Panencephalitis: Influence of the Clinical Course and Treatment with Isoprinosine on Non-Specific Cell-Mediated and Humoral Immunity

M. Vainiene, A. Czonkowska and J. Korlak. Acta Neurol Scand 1983 May;67(5):275-84.

Authors' abstract: Cell-mediated and humoral immunity were studied in 30 patients with subacute scleros-

ing panencephalitis (SSPE). Marked changes in cell-mediated immunity were observed, manifested as a decrease in total lymphocyte count, decrease of proportion of T cells forming late E rosettes, depression in lymphocyte blastogenesis, production of migration inhibition factor and delayed-type skin reactivity. The humoral immune responses were not so markedly changed and only increased levels of serum IgG, IgM and the C3c fragment of complement were noticed. The changes in immunity were more pronounced in patients with a more advanced stage of the disease. 19 patients were investigated 3 times at 7-week intervals during treatment with isoprinosine. In the group of patients (10 cases) whose clinical status was rapidly deteriorating, a marked decline of cell-mediated immunity was observed. In the group of patients showing a stationary course of the disease, cellular immunity was improving. The mechanism of the disturbances of non-specific immunity in SSPE and the influence of isoprinosine on the immune answer are discussed.

Radioimmunoassay of Measles Virus Antibodies in SSPE

M.A. Jankowski, W. Gut and M. Kantoch. Acta Virol (Praha) 1982 Dec;26(6):481-7.

Authors' abstract: A sensitive radioimmunological assay (RIA) was introduced for detection of measles virus IgG and IgM antibodies. The hyperimmune response to measles virus could be demonstrated more precisely by RIA than by hemagglutination inhibition (HI). The ratio between RIA and HI antibody titers was decidedly higher in sera and cerebrospinal fluids (CSF) of patients with subacute sclerosing panencephalitis (SSPE) than in those of other groups tested.

How Does Anti-Measles Vaccination Influence the Incidence of Subacute Sclerosing Panencephalitis? (Hebrew)

E. Kahana, L. Rannon and N. Zilber. Harefuah 1982 Nov 15;103(10):261-3.

English summary: In a country-wide survey of subacute sclerosing panencephalitis (SSPE) in Israel, 110 cases were identified. These included patients born before and after the institution of mass anti-measles vaccination in Israel in 1967. Most of the patients reported measles at a significantly younger age than the general population (95% before the age of five and 70% before the age of two) regardless of whether they were born before or after the institution of mass anti-measles vaccination. Ten years after the institution of mass immunization the incidence of SSPE in Israel began to decrease. This decrease could not be explained by any problem in case finding or diagnosis. The incidence of SSPE was 628 per million of estimated measles cases below the age of five. The rate in vaccinated children was only 8-27 per million, 23-78 times less than after measles infection.

There is strong evidence that SSPE is connected with early measles infection, and by altering the epidemiology of measles, anti-measles vaccination influences its prevalence. The appearance of SSPE in some vaccinated patients may be explained by the fact that the efficacy of the vaccine is not 100% and the possibility of undiagnosed infection by wild measles virus before vaccination.

Measles, Measles Vaccination, and Risk of Subacute Sclerosing Panencephalitis (SSPE)

N. Zilber, L. Rannon, M. Alter and E. Kahana. Neurology (NY) 1983 Dec;33(12):1558-64.

Authors' abstract: Between the years 1968 and 1979, 87 cases of subacute sclerosing panencephalitis (SSPE) appeared among the Israeli-born population. The incidence of SSPE dropped sharply in 1977, 10 years (the median age at onset of SSPE) after introduction of mass antimeasles vaccination, and remained low in 1978 and 1979. Most of the SSPE cases reported measles at an age significantly younger than that of the general population. This pattern did not change after introduction of antimeasles vaccination. Incidence was significantly lower ($p < 10^{-9}$) in the vaccinated population than in the unvaccinated population. Occurrence of SSPE in some children who were vaccinated against measles could be explained by incomplete vaccine efficacy, or by older age at vaccination, which allows the possibility of prior exposure to measles. There was no indication that measles vaccine can induce SSPE.

Epidemiology of Subacute Sclerosing Panencephalitis (SSPE) in Romania Between 1976-1982

C. Cernescu and S. Milea. Virologie 1983 Oct-Dec;34(4):239-50.

Authors' abstract: The analysis of 415 SSPE cases detected between 1976-1982 pointed out a relatively high yearly incidence of this disease: 5-6 cases per 1 million inhabitants. Clusters of SSPE cases were observed in certain counties of Romania. The onset of SSPE occurred mostly at 6-7 years (only 6% of the cases were detected in children over 10 years of age); the mean duration of the interval between acute measles and SSPE onset was of 4-5 years. The following risk factors were made evident in the patients' past histories: male sex, acute measles experienced under the age of 1-2 years, existence of several siblings, long time intervals spent in the rural environment or in child communities, contact with domestic animals. During the first three years of its application on a national scale antimeasles vaccination had no effect on SSPE incidence.

An Epidemiological Study of Subacute Sclerosing Panencephalitis in Kenya

P.M. Tukei, P.R. Kenya and H. Ensering. East Afr Med J 1983 Jan;60(1):34-8.

Authors' summary: Twenty-one cases of SSPE were clinically and serologically confirmed within Kenyatta National Hospital during 1978 and 1979. The majority of the cases were between 5-9 years of age. The mean age at onset was 7.1 years with a male:female ratio of 2.1.

A previous history of clinical measles was positive in 76% of the cases. No tribal preponderance was evident. It is suggested that SSPE in tropical countries similar to Kenya may not be as uncommon as has hitherto been thought.

Subacute Sclerosing Panencephalitis in Only One of Identical Twins. Case Report with Study of Cell-Mediated Immunity

C. Cianchetti, M.G. Marrosu, P.E. Manconi, M. Loi and A. Cao. Eur Neurol 1983;22(6):428-32.

Authors' abstract: A case of identical twins is reported in which only 1 was affected by subacute sclerosing panencephalitis. The affected twin showed a defect of cellular immunity, mainly a decrease of T lymphocytes. This defect therefore appears to be a consequence and not a genetic determinant of the disease.

Familial Occurrence of Subacute Sclerosing Panencephalitis (SSPE) in Children (Polish)

R. Michaowicz, R. Ignatowicz and M. Kostrzewska. Neurol Neurochir Pol 1983 Nov-Dec;17(6):651-4.

English summary: The authors discuss the etiology and pathogenesis of SSPE in the light of own observations of two boys aged 8 and 9 years whose one grandfather and one grandmother were siblings. The boys lived in different parts of Poland and had never been in contact with each other. In the light of this observation the authors discuss the possibility of a genetic background in SSPE.

Tuberculosis

Management of Tuberculin Reactors in Children and Adolescents Previously Vaccinated with BCG

R.L. Nemir and A. Teichner. Pediatr Infect Dis 1983 Nov-Dec;2(6):446-51.

Authors' abstract: Between 1960 and 1981, 142 Bacillus Calmette-Guerin (BCG)-vaccinated children and adolescents were evaluated in the Children's Chest Clinic, Bellevue Hospital. These patients came from 28 countries and had positive tuberculin reactions and/or exposure to active tuberculosis. Antituberculous therapy was given to 8 with active tuberculosis, to 8 with calcified pulmonary primary lesions and to 105 positive tuberculin reactors without disease. In a 1½- to 16-year follow-up, no tuberculous disease occurred, and two patients with previously negative roentgenograms developed calcified pulmonary lesions. Guidelines are given for the management of patients previously vaccinated with BCG with special reference to the value of prophylactic isoniazid therapy for those considered infected by *Mycobacterium tuberculosis* but without evidence of disease.

Tuberculosis Screening

P. Murata and R.A. Johnson. Am Fam Physician 1984 Mar;29(3):247-53.

Authors' abstract: In view of the decreasing prevalence of tuberculosis, it is important to be aware of the factors influencing the sensitivity, specificity and predictive value of tuberculin testing. The small predictive value of tuberculin testing in a low-risk population makes it an ineffective means for screening. Even in high-risk populations, factors such as geographic location, reaction size, previous skin testing and BCG vaccination significantly influence interpretation of the skin test.

Tuberculous Manifestations in Children

M.B. Ragha, Y.S. Patel, C. Chintu and V. Chawla. Med J Zambia 1980 Jun-Jul;14(4):53-6.

Authors' abstract: An analysis of 110 cases of primary tuberculosis in Zambian children revealed that 47% of them had protein energy malnutrition. Of all pulmonary manifestations, simple primary tuberculosis was predominant followed by segmental lesions. A high incidence of extrapulmonary involvement, mainly tuberculous lymphadenitis, was observed. Previous BCG inoculation was not protective in 37 (33.6%) children.

Tuberculosis in Unvaccinated Children, Adolescents, and Young Adults: A City Epidemic

J.D. Hill and D.K. Stevenson. Br Med J [Clin Res] 1983 May 7;286(6376):1471-3.

Authors' abstract: In an epidemic of tuberculosis, 41 new patients presented with the disease or were traced. The index patient was a part-time barman in a public house. Four children in his family and four who lived in the same block of flats were infected. Only seven of the 41 patients had been vaccinated with BCG. This epidemic indicates that the schools vaccination program should be continued and the public made aware that tuberculosis still exists.

The BCG Controversy. A Methodological and Statistical Reappraisal

J.D. Clemens, J.J. Chuong and A.R. Feinstein. JAMA 1983 May 6;249(17):2362-9.

Authors' abstract: Because of the conflicting results of eight major controlled trials, BCG vaccination against tuberculosis remains controversial despite more than 50 years of use. Suspecting a methodological source for the controversy, we reviewed the scientific and statistical quality of each trial. The analysis showed that (1) although biased allocation of the vaccine appeared an unlikely explanation for the disparate results, adequate demonstration of unbiased detection of tuberculosis was available only for the three trials reporting 75% or greater protective efficacy; and (2) in most trials reporting low efficacy, the results had wide confidence intervals that could not exclude high efficacy, but the trials reporting high efficacy all had narrow confidence intervals that excluded low efficacy. Because the trials with the best methodological quality and greatest statistical precision reported high efficacy, the evidence suggests that BCG can confer a high degree of protection against tuberculosis and that bias or inadequate statistical power may have contributed to the conflicting data.

Incidence of Childhood Tuberculosis After Neonatal BCG Vaccination

H.M. Curtis, I. Leck and F.N. Bamford. Lancet 1984 Jan 21;1(8369):145-8.

Authors' abstract: Neonatal BCG vaccination has long been offered routinely to children born at St Mary's Hospital (SMH), Manchester, England, whereas the city's other obstetric hospitals have generally restricted this procedure to children of Asian origin and those with a family history of tuberculosis. Among children aged 0-14 years who had been born to Manchester residents in 1965-80, 65 presented with tuberculosis in 1975-80 whilst still resident in the city. The estimated incidence rate was less than half as high among all children born at SMH as among those not born there, largely because the rate for those born and vaccinated at SMH was less than one-quarter of that for those born elsewhere. Children with Bangladeshi, Indian, or Pakistani surnames also shared in the reduced risk associated with vaccination. These findings strongly support the effectiveness of neonatal BCG vaccination.

BCG Vaccination as a Cause of Multifocal Osteomyelitis in a 12-Year-Old Girl

C. Moell, T. Wiebe and T. Hallberg. Acta Paediatr Scand 1983 Jan;72(1):153-5.

Authors' abstract: A 12-year-old girl with multifocal skeletal sclerosis has been investigated. She was BCG vaccinated at birth and developed regional lymphadenitis in her left groin at two months of age. She was healthy until approximately 10 years of age, after which deficient height and weight gain occurred. BCG-itis was diagnosed in skeleton lesions. No evidence of immunodeficiency was found in the patient. After antituberculous treatment, the skeleton lesions, previously seen at bone scan, had disappeared. There has been a dramatic effect on her weight gain, growth and general well-being.

Varicella-Zoster Infections

Immunologic Evidence of Reinfection with Varicella-Zoster Virus

A.M. Arvin, C.M. Koropchak and A.E. Wittek. J Infect Dis 1983 Aug;148(2):200-5.

Authors' abstract: Resistance to reinfection with varicella-zoster virus (VZV) was evaluated in immune adults who had household exposure to varicella. Sixty-four percent of 25 adults exposed to varicella had a fourfold or greater rise in IgG antibody to VZV or had a high initial IgG antibody titer to VZV that declined by fourfold. IgM antibody was detected in only 12% of 25 VZV-immune subjects. Seventy percent of 23 subjects exposed to varicella had IgA antibody to VZV compared with 13% of 23 subjects with antibody to VZV who had no recent exposure ($p<0.001$, chi 2 test). Enhanced cellular immunity was documented by an increase in lymphocyte transformation to VZV antigen from a mean ± SE index of 7.8 ± 1.30 to 15.3 ± 2.56 ($p=0.01$, paired t-test). The increase in immunity to VZV in many immune subjects exposed to VZV suggests the occurrence of subclinical reinfection.

Clinical Reinfection with Varicella-Zoster Virus

A.A. Gershon, S.P. Steinberg and L. Gelb. J Infect Dis 1984 Feb;149(2):137-42.

Authors' abstract: Eight patients became clinically reinfected with varicella-zoster virus despite the presence of specific antibody in the blood three days to six months before the onset of illness. One patient had had varicella previously; a second had been immunized with live Gelb, attenuated varicella vaccine 10 months earlier. While it was suspected that these patients experienced a reactivation of latent virus that caused atypical disseminated zoster rather than varicella, detailed study of the vaccinated child suggests that this was not the case; by restriction-endonuclease techniques, this vaccinee was shown to have been infected with wild-type varicella-zoster virus despite the presence of specific antibody and cellular immunity to the virus. All cases clinically resembled chickenpox. Thus, not only subclinical varicella (manifested by a rise in antibody titer after close exposure) but also clinical reinfection with the virus can occur. Clinical rein-

fection probably develops more frequently in immunocompromised than in immunocompetent individuals. Reinfections are usually mild.

Enzyme-Linked Immunosorbent Assay for Susceptibility to Varicella

Z. Shehab and P.A. Brunell. J Infect Dis 1983 Sep;148(3):472-6.

Authors' abstract: Nonspecific reactions to the membrane antigen of varicella-zoster virus were found by fluorescent antibody assay in the sera of three children susceptible to the virus; one of these children subsequently developed varicella. None of the three sera, however, contained antibody to varicella-zoster virus that was detectable by enzyme-linked immunosorbent assay (ELISA). Moreover, the results of the ELISA clearly distinguished immune from susceptible individuals. The negative range was established with sera obtained from 15 individuals prior to the onset of varicella, and the positive range was established with sera obtained from 75 healthy donors with a history of varicella. The results of the ELISA correlated well with those of the fluorescent antibody assay ($r = +0.84$). Heterologous reactions to herpes simplex virus were found in one of seven sera tested, and such reactions to cytomegalovirus were found in two of five sera. Heterologous reactions to Epstein-Barr virus were found in none of eight sera tested. ELISA is easy, sensitive, and reproducible and can be used for routine screening for susceptibility to varicella.

Herpes Zoster Causing Varicella (Chickenpox) in Hospital Employees: Cost of a Casual Attitude

P.J. Hyams, M.C. Stuewe and V. Heitzer. Am J Infect Control 1984 Feb;12(1):2-5.

Authors' abstract: Varicella is a benign exanthematous disease of childhood, with adult infection usually occurring in the immunocompromised patient. Hospital employees may be exposed to the varicella virus through contact with patients having either varicella or herpes zoster. Two nurses developed varicella 11 and 15 days after contact with a patient with disseminated herpes zoster. Twenty-five susceptible employees were excluded from work. The cost to the hospital for this paid leave was $10,941. Additional nurses were hired to staff the 189 uncovered supplementary nursing shifts; the accrued cost was $8,093. Ninety patients were exposed. There were no secondary cases in either employees or patients. Nosocomial varicella in hospital employees can be both costly to the hospital and disruptive of patient care. Measures to prevent such an occurrence are discussed.

Susceptibility to Varicella Virus of Certain Adults in the Southeastern United States

P.J. Hyams, S. Vernon and D. Eckert. Am J Infect Control 1984 Feb;12(1):6-9.

Authors' abstract: The serologic status of 76 adults was determined to evaluate their immunity to the varicella virus. Previous reports indicate that 92% to 98% of the adult population develop this immunity. Our experience with nosocomial varicella infection in two hospital employees suggested that more adults in this subtropical region may be susceptible to varicella infection. Three (7.1%) adults with a definite history of varicella had a positive indirect fluorescent antibody (IFA) test. Twenty-eight (72%) of 39 employees without a history had a positive serology, a rate lower than previously reported ($p < 0.002$). Twenty-nine (85%) of 34 other adults and 60 (79%) of the 76 adults tested had positive tests; these rates are also lower than reported ($p = 0.003$ and < 0.001, respectively). These data indicate that some adult groups may be more susceptible to varicella infection and suggest that knowledge of immunity should be an important health concern in some hospitals.

Clinical Trial of Live Attenuated Varicella Vaccine in High-Risk Susceptibles—A Preliminary Report

A.A. Gershon, S. Steinberg, W. Borkowsky and the NIH Collaborative Study Group. Dev Biol Stand 1982;52: 391-7.

Authors' conclusion: Seventy-nine subjects have been immunized with live attenuated VZ vaccine (Oka strain), including 18 normal susceptible adults, 26 leukemic children whose chemotherapy had been terminated for, on the average, 6 months, and 35 leukemic children in remission for at least 1 year but with chemotherapy suspended for 2 weeks. All subjects have responded immunologically to the vaccine with development of VZ antibody and CMI. Side effects have been mild. For adults and leukemics whose chemotherapy was terminated, side effects have been rare and limited to a few papular lesions. Leukemic children whose chemotherapy was suspended have had an incidence of rash of 54%, but no rash could be considered even moderately severe. Three children had rashes with some characteristics of mild zoster about 2 months after vaccination. Fever occurred in only 3% and lasted only 1-2 days. No evidence of shedding or spread of vaccine virus to others has been found although VZ virus was isolated from the lesions of one child with rash. Thus far four adults and four leukemic children whose chemotherapy was finished have been closely exposed to VZ virus and none has developed varicella as a result of these exposures. Immunity to VZ virus has been persistent in all vaccinees, with the longest follow-up being 3 years. This experience suggests that vaccination against varicella may be achieved safely, even in high-risk children, and that the vaccine is highly immunogenic. It

is expected that as more children are enrolled in this ongoing study additional important information regarding vaccine safety efficacy will emerge.

Five-Year Follow-Up Study of Recipients of Live Varicella Vaccine Using Enhanced Neutralization and Fluorescent Antibody Membrane Antigen Assays

Y. Asano, P. Albrecht, L.K. Vujcic, G.V. Quinnan, Jr., K. Kawakami and M. Takahashi. Pediatrics 1983 Sep;72 (3):291-4.

Authors' abstract: Twenty-six healthy children susceptible to varicella were inoculated with the OKA strain of live attenuated varicella vaccine. All of the recipients showed good antibody responses without adverse clinical reactions. The seropositivity rate 5 years after vaccination was 100% by the enhanced neutralization test and 96% by the fluorescent antibody membrane antigen (FAMA) test. None of the recipients contracted varicella in spite of documented contact exposure. None of the children developed herpes zoster during the 5-year observation period. The results suggest that attenuated varicella vaccine has long-term protective efficacy.

Preliminary Study of an Attenuated Varicella-Zoster Vaccine (Webster Strain) in 27 Children Without Immunologic Disorders (French)

B. Hediard, A.M. Burguiere, A. Devillechabrolle, S. Lemerle, P. Reinert, S.A. Plotkin and J.M. Huraux. Ann Pediatr (Paris) 1983 Jun;30(6):440-4.

English summary: Following Takahashi's studies of the Oka strain varicella-zoster vaccine we have investigated the clinical tolerance and effectiveness of the Webster strain. This strain was obtained by Plotkin from a strain recovered from a child with varicella and passed seventy times on human diploid WI 38 cells. Twenty-seven susceptible children without overt immunological disorders were vaccinated. Daily clinial evaluation for at least 28 days showed that tolerance was satisfactory: no child had a vesiculous eruption during the month which followed immunization. Seroconversion was demonstrated in 96% of cases with FAMA-test, but in only half the cases with the complement fixation or the ELISA test. Follow-up, which was at least six months and, in some instances, 1 or 2 years showed that, although antibodies were transient, relative protection was ensured: only one of the 9 children acknowledgedly exposed exhibited a varicelli-form eruption and 5 of the 7 children who had serologic tests after exposure showed evidence of latent infection. Our findings seem to indicate that the Webster strain might reasonably be experimented with in immunocompromised children if immunization with an alternative strain, more attenuated than the Oka strain, seems required.

Evaluation of Varicella-Zoster Immune Globulin: Protection of Immunosuppressed Children After Household Exposure to Varicella

J.A. Zaia, M.J. Levin, S.R. Preblud, J. Leszczynski, G.G. Wright, R.J. Ellis, A.C. Curtis, M.A. Valerio and J. LeGore. J Infect Dis 1983 Apr;147(4):737-43.

Authors' abstract: Varicella-zoster immune globulin (VZIG), an immunoglobulin prepared from normal donor plasma selected for high titer of antibody to varicella-zoster virus (VZV), and zoster immune globulin (ZIG), prepared from the plasma of donors convalescing from herpes zoster, were compared in a double-blind, randomized clinical trial to determine their relative efficacy in protecting immunosuppressed children from severe varicella. VZV infection occurred in 49 (60.4%) of 81 recipients of VZIG and in 57 (68.6%) of 83 recipients of ZIG. These rates and the clinical severity of varicella were not significantly different; however, the subclinical infection rate was significantly higher in ZIG recipients (31.3% vs. 16.0%). This difference was accounted for by a subgroup of patients receiving immunosuppressive therapy for nonneoplastic diseases. Doubling the dose of VZIG administered reduced the rate of subclinical infection. These data indicate that VZIG can be used to protect immunosuppressed children from severe chickenpox.

Varicella Zoster Virus Antibody Titers Before and After Administration of Zoster Immune Globulin to Neonates in an Intensive Care Nursery

E.E.L. Wang, C.G. Prober and A.M. Arvin. J Pediatr 1983 Jul;103(1):113-4.

From authors' discussion: Thirty-two infants in our intensive care nursery who were exposed to varicella zoster virus (VZV) were given zoster immune globulin (ZIG) intramuscularly within 72 hours after exposure. All infants were less than 2 months of age. Their gestational ages ranged from 25 to 40 weeks, and their birth weights ranged from 750 to 4790 gm. No clinical cases of varicella were detected during the six-week study period. Thirty-one of 32 patients had detectable VZV antibody before ZIG administration. The lowest mean VZV antibody titer was observed in infants whose gestational age was 25 weeks or less. Infants of 26 to 30 weeks' gestation had VZV antibody equivalent to those in the infants of more than 30 weeks gestation. The infants weighing 1000 gm or less tended to have lower VZV antibody titers than infants of higher birth weight. The authors suggest that it is not necessary to administer VZV antibody to all premature or sick infants who are inadvertently exposed to VZV. Their results indicate that infants with birth weights of 1000 gm or less or gestational ages less than 25 weeks may have low or undetectable antibody to VZV. If exposure to VZV occurs in a nursery, infants of very low birth weight and gestational age should be screened for VZV antibody. If antibody screening is not feasible, ZIG administration may be limited to this group.

Viral Hepatitis

Progress Toward a Live Attenuated Human Hepatitis A Virus Vaccine

M.R. Hilleman, P.J. Provost, E.B. Buynak and A.A. McLean. Dev Biol Stand 1983;54:433-40.

Authors' abstract: Human hepatitis A virus (HAV) was first grown in cell cultures four and one-half years ago, enabling significant progress toward the development of HAV vaccines. Vaccine development in a number of laboratories has proceeded on three fronts: 1) live, attenuated vaccine of cell culture origin; 2) inactivated vaccine of cell culture origin; and 3) genetic recombinant vaccines. Our studies to date have focused most heavily on the development of a live, attenuated HAV vaccine, although we have also made a prototype killed HAV vaccine from infected marmoset liver which induced anti-HAV and solid immunity to infection in marmosets. HAV was attenuated in virulence for both marmosets and chimpanzees by serial passaging in fetal rhesus monkey kidney cells and human diploid embryonic lung fibroblasts. A number of variants were produced which showed different levels of virulence/attenuation in these animal models. Some variants showed desirable live vaccine-like properties (little or no induction of enzyme elevations; little or no liver histologic change; retention of anti-HAV induction capacity). Vaccinated animals were solidly immune to challenge with virulent HAV. Experimental vaccines have been prepared from several attenuated HAV variants and preliminary studies in humans are planned.

Subcutaneous Administration of Inactivated Hepatitis B Vaccine by Automatic Jet Injection

S.M. Lemon, R.M. Scott and W.H. Bancroft: J Med Virol 1983;12(2):129-36.

Authors' abstract: To assess the feasibility of jet injection for mass immunization against hepatitis B virus, inactivated, alum-adsorbed hepatitis B vaccine (Merck Sharp & Dohme Research Laboratories, West Point, PA) was administered subcutaneously by automatic jet injection to 19 volunteers lacking antibody to hepatitis B surface antigen (anti-HBs). Three 20-microgram doses were given at 0, 1, and 6 months. Of 19 volunteers, 5 (26%) developed anti-HBs by 1 month after the first injection, and 15 of 19 (79%) were anti-HBs-positive 6 to 8 weeks after the first booster administration. Following the second booster, 16 of 19 (84%) recipients had detectable anti-HBs. Possible systemic reactions were limited to low-grade fever (37.8° C) in one volunteer following one injection, and mild lethargy in a second recipient. Local reactions to jet injection of vaccine occurred more frequently, with indurated, nodular lesions 3-10 mm in diameter developing at the site of 19 of 57 (33%) vaccine injections, compared with 2 of 57 (3%) saline placebo injections. Such nodules were generally painless. Sore arms were noted in 11 of 57 (19%) vaccine injections. With the exception of frequent but minor local reactions, subcutaneous administration of inactivated hepatitis B vaccine by automatic jet injection is safe, and results in vaccine immunogenicity approximating that associated with intramuscular needle injection.

Simultaneous Administration of Hepatitis B and Diphtheria/Tetanus/Polio Vaccines (Letter)

J.P. Chiron, P. Coursaget, B. Yvonnet, F. Auger, T. Lee Quan, F. Marin, F. Denis and I. Diop-Mar. Lancet 1984 Mar 17;1(8377):623-4.

From authors' discussion: We investigated the immune response to HBsAg and tetanus toxoid antigen when administered simultaneously as hepatitis B vaccine and DT-polio vaccine to Senegalese children aged 3-24 months. One group of children received hepatitis B vaccine, a second group DT-polio vaccine, and a third group (DT-polio + HB vaccine) was given both vaccines simultaneously but in different arms. For all three groups the injections were repeated at 1 and at 2 months.

One month after the second injection of vaccine 43 infants from the DT-polio vaccine group and 42 from the DT-polio + HB vaccine group were investigated for tetanus toxoid antibodies. All infants had anti-tetanus toxoid antibody and no difference in the geometric mean titer was observed (977 and 1233 mIU/ml, respectively).

The HB vaccine immune response was investigated only in children who were seronegative or had anti-HBc alone at the time of the first injection of vaccine. At the time of the third injection anti-HBs was detected in 47 out of 50 infants from the DT-polio + HB group (97%). The proportion of high anti-HBs titers (> 200 mIU/ml) was 6% in the hepatitis B vaccine group and 13% in those receiving both vaccines (this difference was not significant). Two months after the third injection of vaccines, anti-HB antibodies were detected in 64 out of 65 infants from the HB vaccine group (93%). No difference was observed in the proportion of high anti-HBs titers (55% and 50%, respectively).

Thus the immune response to HBs and tetanus toxoid antigens observed after immunization of infants with HB vaccine and DT-polio vaccine in combination was at least equal to the immune response observed after administration of these vaccines alone.

A New Hepatitis B Vaccine Containing HBeAg in Addition to HBsAg

A.M. Prince, J. Vnek and W. Stephan. Dev Biol Stand 1983;54:13-22.

Authors' abstract: A new vaccine is reported which contains HBeAg in addition to highly purified HBsAg. The rationale for this approach depends on the following

data indicating that anti-HBe/anti-HBc may play an active role in prevention of HBV infection; (1) active immunization of chimpanzees with HBeAg(s) devoid of detectable HBsAg protected against subsequent challenge with HBV; (2) passive immunization of chimpanzees with an anti-HBe/anti-HBc intravenous immunoglobulin devoid of anti-HBs significantly delayed and appeared to attenuate HBV infection following subsequent challenge with HBV. The purification procedure utilized for production of the NYBC vaccine was designed to accomplish a high degree of purification with minimal use of complex equipment. This may facilitate eventual utilization of the vaccine on a mass scale for prevention of the HBV carrier state in high prevalence regions of the world. This procedure uses PEG precipitations and hydroxylapatite adsorption steps, followed by only a single isopycnic separation in a zonal rotor, to achieve a vaccine which is substantially free of serum proteins and detectable HBV DNA yet contains immunogenic quantities of HBsAg and HBeAg. The vaccine is inactivated by Tween 80 and formalin. Four lots have passed chimpanzee safety tests; two of them have been tested in clinical trials.

Vaccine Against Human Hepatitis B Virus Prepared from Antigen Derived from Human Hepatoma Cells in Culture

W.J. McAleer, H.Z. Markus, D.E. Wampler, E.B. Buynak, W.J. Miller, R.E. Weibel, A.A. McLean and M.R. Hilleman. Proc Soc Exp Biol Med 1984 Mar;175(3):314-9.

Authors' abstract: Vaccine against human hepatitis B was prepared using antigen derived from hepatitis B carrier hepatoma cells grown in the interstices of a Diaflo hollow filter unit. Hepatitis B surface antigen (HBsAg) produced by these cells was purified by immune affinity chromatography, digestion with DNase and pepsin, and Sephadex G-150 separation. The Formalin-treated antigen was formulated in 20-micrograms dose on alum adjuvant with thimerosal added as a preservative. This cell culture vaccine was as potent as human plasma-derived vaccine as measured in a mouse potency assay. The vaccine proved safe in tests in chimpanzees and in human subjects who were in late stages of cancer of the central nervous system and who were receiving therapy for their condition. None of five subjects who received the vaccine developed untoward clinical reactions. Two of the subjects who received all three doses of vaccine developed antibody against HBsAg. Three persons, two given only the primary doses and one who was given all three doses but was lost to follow-up, demonstrated no response. The slow and relatively low antibody responses to the vaccine were similar to those in other immunosuppressed persons who were given vaccine of human plasma origin.

Human Hepatitis B Vaccine from Recombinant Yeast

W.J. McAleer, E.B. Buynak, R.Z. Maigetter, D.E. Wampler, W.J. Miller and M.R. Hilleman. Nature 1984 Jan 12-18;307(5947):178-80.

Authors' abstract: The worldwide importance of human hepatitis B virus infection and the toll it takes in chronic liver disease, cirrhosis and hepatocarcinoma, make it imperative that a vaccine be developed for worldwide application. Human hepatitis B vaccines are presently prepared using hepatitis B surface antigen (HBsAg) that is purified from the plasma of human carriers of hepatitis B virus infection. The preparation of hepatitis B vaccine from a human source is restricted by the available supply of infected human plasma and by the need to apply stringent processes that purify the antigen and render it free of infectious hepatitis B virus and other possible living agents that might be present in the plasma. Joint efforts between our laboratories and those of Drs. W. Rutter and B. Hall led to the preparation of vectors carrying the DNA sequence for HBsAg and antigen expression in the yeast *Saccharomyces cerevisiae*. Here we describe the development of hepatitis B vaccine of yeast cell origin. HBsAg of subtype *adw* was produced in recombinant yeast cell culture, and the purified antigen in alum formulation stimulated production of antibody in mice, grivet monkeys and chimpanzees. Vaccinated chimpanzees were totally protected when challenged intravenously with either homologous or heterologous subtype *adr* and *ayw* virus of human serum source. This is the first example of a vaccine produced from recombinant cells which is effective against a human viral infection.

Hepatitis B Surface Antigen (HBsAg) Subtype-Specific Antibodies in Persons Vaccinated Against Hepatitis B

W. Jilg, C. Delhoune, F. Deinhardt, A.J. Roumeliotou-Karayannis, G.J. Papaevangelou, I.K. Mushahwar and L.R. Overby. J Med Virol 1984;13(2):171-8.

Authors' abstract: One hundred sixty-three persons immunized against hepatitis B with a vaccine containing HBsAg either of *adw* or *ayw* subtype were examined for antibodies against the *a*, *d*, and *y* determinants of HBsAg. Sera were tested for antibodies against HBsAg *adw* and HBsAg *ayw* separately by a solid-phase radioimmunoassay using polystyrene beads coated with HBsAg of either *adw* or *ayw* subtype, and the relative amounts of antibodies against the single determinants were calculated. After the third immunization, all vaccinees had antibodies against the common determinant *a*. A quantitative evaluation showed that on average about 50% of HBsAg-specific antibodies were directed against the *a* determinant, and about 50% against *d* or *y*, respectively. However, as only anti-*a* is protective against cross-infection with other HBsAg subtypes, the degree of im-

munity of a person vaccinated against hepatitis B should be evaluated by the determination of antibodies to *a* rather than antibodies against total HBsAg.

Hepatitis B Vaccine: Clinical Trials in High-Risk Settings in France (September 1975-September 1982)

A. Goudeau, F. Dubois, F. Barin, M.C. Dubois and P. Coursaget. Dev Biol Stand 1983;54:267-84.

Authors' abstract: An alum bivalent hepatitis B vaccine containing 5 micrograms/dose of formalin-inactivated and purified HBsAg has been prepared from plasma of HBeAg negative donors. Safety of the product has been controlled by compulsory testing of each batch in susceptible chimpanzees. This vaccine (HB vaccine) was used for the prophylaxis of hepatitis B in hospital staff working in high-risk settings and patients undergoing periodic dialysis since the autumn of 1975. Tolerance to the HB vaccine was excellent both in staff and patients as assessed by a nationwide survey on a thousand vaccinees. More than 96% of the staff developed protective levels of anti-HBs after three injections of vaccine given at one month intervals and became fully immune from HBV infection. A booster injection given at one year stimulated an anamnestic rise of anti-HBs sufficient to ensure protective levels of antibody for at least five years post-booster. The response of renal patients varied according to the age of recipients: young patients responded equally as well as the healthy staff, while patients over the sixth decade had a lower and delayed response. Because of that, a fourth injection of HB vaccine was advocated in elderly patients. Dialysis patients who developed anti-HBs either after three or four injections were fully protected against chronic HBV infections. Anti-HBs positive donors who had received a single booster injection of HB vaccine and vaccinees who had received their 12 months booster were both found to be an adequate source of high-titer anti-HBs plasma for preparing hyperimmune anti-HBs globulin. The HB vaccine which is manufactured by Institut Pasteur Production under the name HEVAC B° is now used world-wide for the prophylaxis of hospital acquired infection in developed countries and for the prevention of maternal-infant transmission in the endemic countries of Asia and Africa.

Preliminary Results of Immune Response to Hepatitis B (HB) Vaccine (Pasteur) in Adults

G. Giunchi, G. Panichi, A. Pescini, M. Pezzella, C. Galli, L.V. Chircu and F. Sorice. Dev Biol Stand 1983;54: 153-9.

Authors' abstract: Antibody responses were estimated in 42 healthy high-risk volunteers submitted to three monthly intradeltoid inoculations of a 5 micrograms HBs vaccine containing both subtypes *adw* and *ayw*. The presence and concentration of anti-HBs varied according to individual responses and the number of injections. One month after the 1st dose those responding numbered 19%, one month after the 2nd the number rose to 83.3%, and reached 100% one month after the 3rd dose. In a few cases antibody levels were low ($\leq$50 mIU/ml), while in most subjects they rose after the 2nd dose, reaching high titers. Concordance and comparability of anti-HBs concentration were achieved by three different measurements (S/N, RIA Units, mIU/ml). No important side effects were observed. The timing of booster doses is discussed.

IgM Antibody Responses to Hepatitis B Surface Antigen in Recipients of Hepatitis B Virus Vaccine

G.Y. Minuk, J.H. Hoofnagle, V.J. McAuliffe and R.H. Purcell. J Infect Dis 1983 Aug;148(2):330.

Authors' abstract: Both total anti-HBs and specific IgM anti-HBs were assayed in sequential serum specimens from five healthy volunteers receiving a primary immunization with the HBV vaccine. Four of the five subjects developed anti-HBs in the six-week period following primary immunization. Anti-HBs was first detectable between days 4 and 21 after initiation of vaccination. Specific IgM anti-HBs was detectable in all four patients who responded to the initial inoculation. This antibody was often present before anti-HBs was detectable by the conventional RIA. However, the titers of IgM anti-HBs were invariably low, and this antibody response was short lived (less than 21 days). The lack of a vigorous and sustained IgM antibody response to HBsAg has also been noted after infection with HBV. This observation is in marked contrast to the magnitude of IgM response to hepatitis B core antigen, which is detectable in high titers during acute HBV infection and persists for months to years after the disease has resolved. The significance of the weak IgM antibody response to HBsAg during both immunization with HBV vaccine and HBV infection is not known but may be related to the relatively low immunogenicity of HBsAg. This weak IgM antibody response may play a role in the propensity of persons with HBV infection to develop the chronic HBsAg carrier state.

Efficacy of a Heat Inactivated Hepatitis B Vaccine in Male Homosexuals: Outcome of a Placebo Controlled Double Blind Trial

R.A. Coutinho, N. Lelie, P. Albrecht-Van Lent, E.E. Reerink-Brongers, L. Stoutjesdijk, P. Dees, J. Nivard, J. Huisman and H.W. Reesink. Br Med J [Clin Res] 1983 Apr 23;286(6374):1305-8.

Authors' abstract: The efficacy of a heat inactivated hepatitis B virus vaccine, containing 3 micrograms hepatitis B surface antigen (HBsAg), was studied in a high-risk group of 800 susceptible homosexual men by a randomized placebo controlled double blind trial. At the trial

end point (21.5 months), 17 hepatitis B virus infections had occurred in vaccinated subjects (attack rate 4.8%) and 56 in subjects receiving a placebo (attack rate 23.8%). This reduction in the incidence of hepatitis B virus infections in vaccinated subjects was highly significant ($p < 0.0001$). Two months after the first injection, 72.3% of the vaccinated subjects had formed antibodies against hepatitis B surface antigen, and this percentage increased to 89% at four months. Maximum anti-HBs titers were reached five months after the first vaccination, the geometric mean titer being 107.6 mIU. Even vaccinated subjects with a low antibody response (≥ 1 and < 10 mIU) were found to be protected from HBsAg-positive infections. The vaccine had no serious side effects.

Hepatitis B Virus Vaccine. An Analysis of Its Potential Use in Medical Workers

J.D. Hamilton. JAMA 1983 Oct 28;250(16):2145-50.

Author's abstract: At the Duke University Medical Center, Durham, NC, there are approximately ten recognized hepatitis B virus (HBV) infections per year in employees. The hospital's hepatitis control program costs $91,995 per year, including costs for workman's compensation, hyperimmune globulin, laboratory tests, lost revenue, liability, personnel, and medical treatment. A program to immunize high-risk medical center personnel and to accommodate residual HBV problems in nonimmunized employees would cost $206,304 in the first year. By seven years the cumulative costs of an immunization program would equal those without a program and at ten years would be cost saving ($746,742 with program vs. $919,950 without a program). Given certain assumptions, HBV vaccine is a cost-beneficial alternative for a major employee health hazard.

Acceptance of Hepatitis B Vaccine Among High-Risk Health Care Workers

A.C. Anderson and G.R. Hodges. Am J Infect Control 1983 Dec;11(6):207-11.

Authors' abstract: During a recent hepatitis B vaccination program among high-risk health care workers, the major sources of information about the vaccine were an in-service informational program, discussion with coworkers, and professional journals. Little or no information was obtained from the lay media or the product brochure. Two thirds of the personnel to whom the vaccine was offered accepted the vaccine. The major reason for accepting the vaccine was a perceived high-risk of contracting hepatitis B. In contrast, one third of the high-risk individuals offered the vaccine declined the opportunity. The major reason for not accepting the vaccine was concern with potential side effects. This information would have been helpful during the planning phase of the program.

Vaccination of Uremic Patients Against Hepatitis B (German)

J. Bommer, F. Deinhardt, W. Jilg, D. Darai, K. Andrassy and E. Ritz. Dtsch Med Wochenschr 1983 Dec 2;108(48):1823-6.

Engiish summary: Hepatitis B vaccine (Merck Sharp & Dohme) was administered according to various vaccination schedules to 12 patients in preterminal renal failure without hemodialysis treatment, 81 patients on a chronic hemodialysis program and 43 staff of a nephrological center. After three doses (at 0, 1, 6 months) of 20 micrograms HBs antigen, seroconversion occurred in 91% of persons without kidney disease. A double dose (40 micrograms) was given, at the same time intervals, to 29 dialysis patients, with a seroconversion rate of 55% and titer levels less than in those without renal disease. Of 26 dialysis patients given the same dose (40 micrograms) five times (at 0, 1, 2, 4, 6 months), 63% achieved seroconversion with a definitely higher anti-HBs titer than those dialysis patients vaccinated only three times. Passive-active vaccination with 40 micrograms HBs antigen (at 0, 1, 2, 4, 6 months) as well as 3 ml hepatitis B immunoglobulin (at 0, 2 months) was given to 26 dialysis patients. There was a comparable frequency of seroconversion (58%) and a comparable titer rise to those obtained with active vaccination alone. Twelve pre-uremic patients not requiring dialysis (serum creatinine 753 ± 184 mumol/l) also were actively vaccinated three times, the results not differing from those in dialysis patients. The findings indicate that patients with renal disease potentially needing dialysis should, in the early stages of renal failure (serum creatinine less than 500 mumol/l) be vaccinated with hepatitis B vaccine.

Efficacy of Heat-Inactivated Hepatitis B Vaccine in Hemodialysis Patients and Staff. Double-Blind Placebo-Controlled Trial

J. Desmyter, J. Colaert, G. De Groote, M. Reynders, E.E. Reerink-Brongers, P.N. Lelie, P.J. Dees and H.W. Reesink. Lancet 1983 Dec 10;2(8363):1323-8.

Authors' abstract: The efficacy of a heat-inactivated hepatitis B vaccine, 3 micrograms of surface antigen (HBsAg), given at 0, 1, 2, and 5 months, was evaluated in 401 hemodialysis patients in 18 centers by a placebo-controlled, double-blind, randomized trial. The attack-rate of hepatitis B virus (HBV) infections in the control group was 18% over 435 days. The protective efficacy rate of the vaccine was 78% against all HBV infections in the entire study ($p = 0.00016$), and 94% against HBsAg-positive hepatitis more than 3 months after day 0. Those patients in whom HBV developed showed no evidence of vaccine-acquired anti-HBs. Among 152 similarly randomized staff members receiving three monthly injections, all 5 HBsAg-positive infections occurred in the placebo group ($p = 0.022$). The vaccine induced anti-HBs in 88%

of the patients and 100% of the staff. Immediately after the fourth injection, anti-HBs levels were as high in responding patients as in staff. There were no serious side effects. In the four-dose schedule the vaccine provides dialysis patients with protection of the same order as that given by other hepatitis B vaccines to normal subjects.

Immunogenicity and Safety of Heat-Inactivated Hepatitis B Vaccine (CLB) in Low Risk Human Volunteers and in Patients Treated with Chronic Hemodialysis in the Netherlands

E.E. Reerink-Brongers, P.N. Lelie, H.W. Reesink, P.J. Dees, H.G. Brummelhuis and W.G. van Aken. Dev Biol Stand 1983;54:197-203.

Authors' abstract: The immunogenicity and safety of a heat-inactivated hepatitis B vaccine (HB-vaccine) were studied in healthy human volunteers (n=471) at a low risk to be infected with hepatitis B virus (HBV) and in patients on chronic hemodialysis (n=227), who were treated in hepatitis B free centers. After vaccination with 3 injections of 3 micrograms heat-inactivated HBsAg adsorbed to $AlPO_4$, given at monthly intervals, 93% of the healthy low risk volunteers had formed anti-HBs. The hemodialysis patients were randomly divided into 2 groups, which were vaccinated with 3 monthly injections of 3 micrograms and 27 micrograms heat-inactivated HBsAg, respectively. It appeared that this 9-fold increase of the vaccine-dosage enhanced the anti-HBs response from 77% in the 3-micrograms vaccinees to 94% in the 27-micrograms recipients. Side-effects of the vaccination were negligible; formation of autoantibodies in consequence of the vaccine treatment was not demonstrated in any of the vaccinees.

Avoidance of Perinatal Transmission of Hepatitis B Virus: Is Passive Immunization Always Necessary?

C. Rosendahl, M.M. Kochen, R. Kretschmer, K. Wegscheider and D. Kaiser. Lancet 1983 May 21;1(8334): 1127-9.

Authors' abstract: Screening of 8918 pregnant women revealed that 107 (1.2%) were HBsAg-positive. 92 of them (50 of German and 42 of predominantly Asian origin) have already delivered and were followed up for 12 months together with their infants. 14 infants of HBeAg-positive (or anti-HBe-negative) carrier mothers received a single dose of hepatitis B immunoglobulin (HBIG) immediately after birth, while 60 infants of anti-HBe-positive mothers were not immunized. 57 of the 60 "unprotected" children remained seronegative for HBsAg and HBeAg. 3 children showed HBs-antigenemia immediately after birth; 2 of these lost HBsAg and developed anti-HBs after 6 and 9 months. The third lost HBsAg after 4 months without an antibody response developing. This suggests that the HBsAg particle only was transmitted rather than the whole virus. 12 of the 14 infants born to HBeAg-positive, or anti-HBe-negative carrier mothers were protected with one single high dose of HBIG. 2 had HBs-antigenemia, 1 had HBeAg as well. These data show that in a West European population the risk of perinatally acquired HBV infection in the infants of anti-HBe-positive carrier mothers is small, and that passive immunization of this group is not necessarily indicated.

Immune Globulin and Hepatitis B Immune Globulin. Prophylactic Measures for Intimate Contacts Exposed to Acute Type B Hepatitis

R.P. Perrillo, C.R. Campbell, S. Strang, C.J. Bodicky and D.J. Costigan. Arch Intern Med 1984 Jan;144(1): 81-5.

Authors' abstract: We studied the relative prophylactic efficacies of recently derived immune globulin containing antibody to hepatitis B surface antigen (anti-HBs) and hepatitis B immune globulin in 60 intimate contacts exposed to acute type B hepatitis. Forty susceptible contacts were randomly assigned to treatment with either a single intramuscular dose of immune globulin or hepatitis B immune globulin (0.06 mL/kg of body weight), following which observation was maintained over a 12-month period. Twenty additional contacts received the equivalent of twice the dose of immune globulin given to the first group, and follow-up was maintained for six months. Neither the hepatitis B virus (HBV) attack rates (11% to 19%) nor the frequency of clinical illness (0% to 4.8%) was substantially different in the three groups. When compared with average frequencies reported in the literature, significantly lower illness rates were noted for immune globulin recipients. These data indicate that currently derived immune globulin as well as hepatitis B immune globulin may confer protection from illness (i.e., passive-active immunity) in the setting of intimate exposure to HBV.

Prevention of Perinatally Transmitted Hepatitis B Virus Infections with Hepatitis B Immune Globulin and Hepatitis B Vaccine

R.P. Beasley, L.Y. Hwang, G.C. Lee, C.C. Lan, C.H. Roan, F.Y. Huang and C.L. Chen. Lancet 1983 Nov 12;2(8359):1099-102.

Authors' abstract: A randomized blind controlled trial of hepatitis B immune globulin (HBIG) plus hepatitis B vaccine for the prevention of the perinatally transmitted HBsAg carrier state was conducted in Taipei. Infants of e-antigen-positive HBsAg carrier mothers were given HBIG immediately after birth, and then one of three schedules of vaccination. There was no difference in efficacy between the three schedules; the combined efficacy was 94%, compared with that of HBIG alone (71%) or of vaccination alone (75%). Persistent HBs antigenemia de-

veloped in only 9 (6%) of the 159 infants receiving prophylaxis, but in 88% of the controls. Antibodies developed in all those who did not become antigenemic and presumably will provide long-term protection from hepatitis B virus infection. HBIG should be given as soon as possible after birth and need not be given again if the infant is subsequently vaccinated. With HBIG coverage from birth, the timing of the start of vaccination does not seem to be of importance within the first month of life, but to maximize compliance and minimize costs hepatitis B vaccination should be initiated during the confinement.

HBIG Prophylaxis for Perinatal HBV Infections—Final Report of the Taiwan Trial

R.P. Beasley, L.Y. Hwang, W. Szmuness, C.E. Stevens, C.C. Lin, F.J. Hsieh, K.Y. Wang and T.S. Sun. Dev Biol Stand 1983;54:363-75.

Authors' abstract: A randomized double blind placebo controlled efficacy trial of hepatitis B immunoglobulin (HBIG) for prevention of the mother to infant transmitted HBsAg carrier state was conducted in Taiwan where the carrier rate in the general population is 15% to 20%. HBIG was given immediately after birth to infants of e-antigen-positive HBsAg carrier mothers and all infants were followed for at least 15 months. Among 61 placebo recipients the carrier rate was 92%; compared with 26% among 57 infants who received 0.5 ml HBIG at birth, three months and six months and 54% among 67 infants who received a single 1.0 ml dose of HBIG at birth only. Efficacy was 71% and 42%, respectively, for the two treatment schedules. The most common response of HBIG-treated infants was passive-active immunization which was 27% in single dose group and 61% in three doses group. Some of the infants who became carriers were probably infected as HBIG protection waned and we expect that higher efficacy can be achieved by HB vaccine in conjunction with HBIG.

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YELLOW FEVER

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VACCINES, TOXOIDS, AND ANTIVIRAL AGENTS

GENERAL

Vaccines and Toxoids

Assessment of the Protective Efficacy of Vaccines Against Common Diseases Using Case-Control and Cohort Studies

P.G. Smith, L.C. Rodrigues and P.E. Fine. Int J Epidemiol 1984 Mar;13(1):87-93.

Authors' abstract: Case-control and cohort studies may be employed to assess the protective efficacy of vaccines. The appropriate measure of vaccine efficacy is shown to depend upon the mode of action of the vaccination. Two models of vaccine action are considered. In the first, vaccination is assumed to reduce the instantaneous disease-rate in the total vaccinated population by a constant proportion and, in the second, vaccination is assumed to render a constant proportion of individuals totally immune from the disease. The implications of these two models on the behavior of different measures of vaccine efficacy in cohort studies is explored. It is shown that the design of case-control studies to measure vaccine efficacy is dependent upon which model is considered appropriate. In particular, under the second model, individuals who have already had the disease under study should not be excluded from the control group.

Synthetic Vaccines

R. Arnon, M. Shapira and C.O. Jacob. J Immunol Methods 1983 Jul 29;61(3):261-73.

Authors' concluding remarks: In view of the above cumulative information, it is apparent that synthetic peptide vaccines may soon become a reality. This approach, if materialized, will have tremendous potential advantages: firstly, it should allow the attachment of several peptides, representing the relevant antigenic portions of different microbial agents, to the same carrier molecule, thus providing multivalent synthetic vaccine. This will necessitate careful modulation of variable parameters in order to overcome the difficulties caused by antigenic competition, but it should be feasible. Secondly, this approach might eliminate the formation of antibodies against many irrelevant microbial antigenic determinants, proteins and other materials, that contaminate the essential immunogen and thereby reduce undesired side effects. Thirdly, it will permit the production of vaccines with built-in adjuvanticity that would be efficient when administered in physiological medium. The key question is, of course, whether synthetic peptides can form the basis for practical vaccines. Thus the critical issues are whether antibodies or the cellular immunity induced by synthetic immunogens will be protective in animals and in man.

The results obtained so far are promising, but problems still remain to be solved. For example, feasibility of identification and production of relevant peptides for every virus or bacteria is not easy to predict. In particular cases, mixtures of more than one of the peptides may be required for an effective synthetic vaccine. Whether chemical synthesis is the optimal procedure or whether genetic engineering should be employed for the synthesis, is another important consideration. In this regard the degree of purity of the peptides required and the size of the peptides to be made will be key factors in deciding which method should be used. The economics of synthetic vaccines also play a role. For example, the case of foot and mouth disease, where a relatively cheap conventional vaccine exists, is very different from hepatitis B where the vaccine available today is of limited availability and very expensive.

Certainly more knowledge is required on the nature and structure of the proteins involved in the process of neutralization of the causative microbial agent. Similarly, important elements requiring more research are the carrier and the adjuvant to be used in the synthetic vaccine. But, in essence the road for the synthesis of vaccines is already paved.

Antibody Response Following Measles-Mumps-Rubella Vaccine Under Conditions of Customary Use

P.A. Brunell, K. Weigle, M.D. Murphy, Z. Shehab and E. Cobb. JAMA 1983 Sep 16;250(11):1409-12.

Authors' abstract: A study of 301 children who had been immunized two to 19 months previously with measles, mumps, and rubella (MMR) vaccine at 36 different sites in San Antonio, Texas, including physicians' offices and clinics, revealed that 99.7% had antibody against rubella and 98.3% had antibody against measles and mumps. None of the 49 infants who were tested prior to receipt of MMR vaccine had antibody against any of these viruses, indicating that the antibody found after immunization was unlikely to be due to false-positive results. The lack of antibody in these infants confirmed that there had not been a significant number of cases of these diseases that could contribute to the high frequency of antibody found after immunization. A single dose of MMR vaccine administered under customary conditions appears to be an effective method of conferring immunity against these diseases.

Effects and Side Effects of a New Trivalent Combined Measles-Mumps-Rubella (MMR) Vaccine

M. Isozaki, H. Kuno-Sakai, N. Hoshi, R. Takesue, I. Takakura, M. Kimura, M. Hikino and M. Mitsuda. Tokai J Exp Clin Med 1982 Sep;7(3):547-50.

Authors' abstract: Effects and side effects of a new measles-mumps-rubella (MMR) vaccine were described. After MMR vaccination, 98% (59/60) of children showed seroconversion by the measles HI test, 98% (65/66) showed seroconversion by the rubella HI test and 57% (34/60) showed seroconversion by mumps NT. Side effects of MMR vaccine were fever (5/82) and skin rash (3/82).

The Safety of Egg-Containing Vaccines for Egg-Allergic Patients

J.R. Miller, H.A. Orgel and E.O. Meltzer. J Allergy Clin Immunol 1983 Jun;71(6):568-73.

Authors' abstract: Forty-two patients with a history of egg sensitivity were evaluated for receiving avian-grown vaccines. After giving a history and undergoing physical examination, each patient was skin-tested with egg antigens and six egg-propagated vaccines, given an oral egg challenge, and finally, when possible, given a vaccine challenge. Thirty-seven of the 42 patients (88%) were ultimately given one or more of the vaccines with no reactions or only minimal ones to both egg protein and vaccine; they had mild reactions consisting of pruritus, headache, and apprehension. Immunization was withheld from three patients who had a history of severe reactions after egg ingestion and strongly positive skin reactivity to both egg and vaccine. A history of egg intolerance should not, by itself, disqualify a patient from receiving one of these vaccines. However, a history of exquisite sensitivity to egg protein indicates that a severe vaccine reaction is likely. An intradermal skin test utilizing 0.02 ml of a 1:100 dilution of the vaccine and resulting in a wheal of greater than 5 mm was found to be the test that most reliably predicted those patients who should not receive the vaccine.

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IMMUNIZATION—GENERAL

General

Mothers' Intentions and the Immunization of Their Infants

P.G.J. Burney. J R Coll Gen Pract 1983 Apr;33(249): 229-32.

Author's summary: One hundred and seventy-eight mothers who had recently been delivered were interviewed before discharge from hospital to ascertain their initial intentions about vaccination of their children. Nine months later the behavior of 154 mothers was checked from health service records; 24 were lost to follow-up.

One hundred and forty-one (92%) of the infants had received at least one dose of vaccine against polio, diphtheria and tetanus. Eighty-five infants (63 percent of 135) had received at least one dose of vaccine against whooping-cough; 19 mothers had been advised against the vaccine. Failure to have their children vaccinated against whooping-cough correlated with the mothers' initial intentions, although a high proportion of mothers who were initially against the vaccine had started vaccination by the time their child was nine months old. Mothers attending general practitioners were more likely to have their infants vaccinated against whooping-cough than those attending community health clinics, and this difference was not explained by the social characteristics of the mothers nor by more positive early intentions among the mothers who attended general practitioners.

Expanded Vaccination Program. Training Model for Community Medicine (French)

C. Gateff. Rev Epidemiol Sante Publique 1983;31(3): 289-98.

English summary: The expanded program on immunization (E.P.I.) is a very concrete example of a community health program. It utilizes various methods which all medical personnel need to learn: the epidemiological method, health planning, and health management. The E.P.I. provides many actual conditions well-suited to the preparing of either tutorials or self-training modules within various fields, such as epidemiological surveys with estimate or evaluation purposes, planning for a prevention strategy, and supply management. Improved community health depends on training. The author points out the importance of making educators aware of the unequalled training opportunities provided by the E.P.I.

Health Care Delivery

Achieving Optimal Immunization Levels in School-Age Children

C. DeAngelis, B. Berman, D. Oda and R. Meeker. J Pediatr 1983 Nov;103(5):811-4.

Authors' abstract: In a school-based immunization program in four states, 70% of the students were fully immunized by the end of the first year and 85% by the end of the second year. Because of student turnover, 20% of the immunization levels achieved by the end of a school year were not sustained into the subsequent year. Levels reported by the state immunization officers were higher than those recorded by school personnel. Completed immunization series for students requiring immunizations were 33% to 40% higher for students enrolled at the start of the year than for students who entered during the school year. Students who were unimmunized at the beginning of the year had a better chance ($p<0.001$) of being immunized by the end of the year than those whose immunization status was unknown. To maintain high levels, a program must be sustained and continuing, provide immunizations, and have careful administrative monitoring of child-specific population-based data. Schools are uniquely able to provide all of these elements, which can augment the efforts of private practitioners.

Preventive Care and Overall Use of Services. Are They Related?

P. Benson, A. Gabriel, H. Katz, D. Steinwachs, J. Hankin and B. Starfield. Am J Dis Child 1984 Jan;138(1):74-8.

Authors' abstract: The relationship between the use of services of children constantly enrolled in a prepaid group practice medical plan for six years and the completeness of their preventive care were examined. Children who were consistently low users of services were more likely to be lacking one or more components of standard preventive care, particularly general health assessments in older children and vision, hearing, and tuberculosis screening in younger children. Teenage children who were low users were at some risk of not receiving their tetanus-diphtheria immunization on time. The relationship between low use of services and incomplete preventive care persisted after controlling for the severity of morbidity, although children with more severe morbidity were somewhat less likely to be missing preventive care. Health facilities and practitioners should pay special attention to assessing the need for standard preventive care in children who are infrequent users of services.

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